EXPERT REPORT OF PROFESSOR IAIN COCKBURN

May 10, 2019

Table of Contents

I. Qualifications

1. My name is Iain M. Cockburn. I am the Richard C. Shipley Professor in Management and Chair of the Strategy and Innovation Department at Boston University's Questrom School of Business. In this capacity, I conduct research on the economics of innovation, with specific application to the pharmaceutical industry, and teach graduate classes on business strategy, competitive analysis, and intellectual property. I also serve as a Research Associate at the National Bureau of Economic Research in Cambridge, Massachusetts. Prior to joining the faculty of Boston University, I held the VanDusen Professorship in Business Administration in the Faculty of Commerce at the University of British Columbia. In addition to these appointments I have also been a Visiting Scholar in the Department of Economics at Harvard University, in the Economics, Finance, and Accounting Department at MIT's Sloan School of Management, and at Melbourne Business School.

2. I received my undergraduate degree from Queen Mary College, University of London in 1984, and my PhD in Economics from Harvard University in 1990.

3. I have served on the Steering Committee for Government Industry Partnerships for the Development of New Technologies of the National Research Council, and on the Scientific Committee of the European Union INNOVPROD Research Network. I have also been a co-editor or referee (an expert in the field that reviews submitted articles and recommends whether or not they should be published) for various academic journals in economics, management, and life sciences, including *Science*, *Journal of Health Economics*, *Health Affairs*, the *British Medical Journal*, *Lancet*, *Management Science*, *Journal of Economics and Management Strategy*, *Journal of Political Economy*, and *American Economic Review*.

4. I have published articles in leading academic journals about my research on various aspects of the pharmaceutical industry, including pharmaceutical pricing, demand estimation, brand-generic substitution, determinants of research productivity and the innovative performance of life sciences companies. My research on the economics of the pharmaceutical industry has been supported by competitive grants from government agencies such as the National Institutes of Health and the National Science Foundation, as well as by private philanthropies and foundations. A complete list of my publications and research grants is included in my curriculum vitae, attached as Appendix A to this report.

5. My research has been cited more than 15,000 times by other scholars, which along with other measures of the impact of my work place me in the top 5 percent of academic economists.

6. Outside academia, I have been a consultant on aspects of public policy related to the pharmaceutical industry to government agencies in the U.S., the U.K., and Canada. I have provided expert testimony in litigation and arbitration matters on issues such as brand-generic competition, pharmaceutical marketing, Medicaid and Medicare reimbursement, licensing and collaboration agreements, patent damages, antitrust, class certification, transfer pricing, and misappropriation of trade secrets. A list of matters in which I have testified at trial or deposition in the past four years is attached as Appendix B.

II. Assignment

7. I have been retained by counsel for Purdue Pharma L.P., Purdue Pharma, Inc., and the Purdue Frederick Company, Inc. (jointly, "Purdue") to review and respond to the reports submitted by the following Plaintiffs' experts: Professors Meredith Rosenthal, David Cutler, Thomas McGuire, Jeffrey Liebman, and Dr. G. Caleb Alexander.[1] Specifically, I have been asked to assess: (1) Professor Rosenthal's methodology for estimating the impact of manufacturer Defendants' allegedly deceptive marketing on prescription opioid sales or shipments;

(2) Professor Cutler's methodology for estimating the impact of prescription opioid shipments on alleged harms; (3) Professor McGuire's methodologies for estimating damages to Plaintiffs, the governments of Cuyahoga and Summit Counties in Ohio ("Plaintiffs"), and public nuisance costs to residents of Cuyahoga and Summit Counties ("Plaintiff Counties"); and (4) Professor Liebman's and Dr. Alexander's methodologies for estimating costs for abating the opioid crisis.

8. For this matter, I am being compensated at my standard billing rate of $850 per hour. I have been assisted in this matter by staff of Cornerstone Research, who worked under my

[1] Expert Report of Professor Meredith Rosenthal, March 25, 2019 ("Rosenthal Report"); Expert Report of Professor David Cutler, March 25, 2019 ("Cutler Report"); Expert Report of Professor Thomas McGuire Damages to Bellwethers, March 25, 2019 ("McGuire Damages Report"); Expert Report of Professor Thomas McGuire Regarding Public Nuisance, March 25, 2019 ("McGuire Public Nuisance Report"); Expert Report of Dr. Jeffrey B. Liebman, March 25, 2019 ("Liebman Initial Report"); Supplemental Expert Report of Dr. Jeffrey B. Liebman, April 3, 2019 ("Liebman Supplemental Report"); G. Caleb Alexander, MD, MS, Expert Witness Report, March 24, 2019 ("Alexander Initial Report"); G. Caleb Alexander, MD, MS, Supplemental Expert Witness Report, April 3, 2019 ("Alexander Supplemental Report").

direction. I receive compensation from Cornerstone Research based on its collected staff billings for supporting my work in this matter. Neither my compensation in this matter nor my compensation from Cornerstone Research is in any way contingent or based on the content of my opinions or the outcome of this or any other matter.

9. In forming my opinions and conclusions, I have reviewed and considered the materials cited herein, such as data and documents produced in this litigation, as well as documents and data provided to me by Purdue, and other publicly available data and documents. The full list of materials I have considered is attached as Appendix C. I have also relied on my years of academic and professional experience as an economist, including my experience in pharmaceutical economics. Although I have set forth citations to certain evidence supporting the analyses in this report, I may also rely upon any evidence from the materials that have been produced by the parties in this action, or that I consider relevant to the task assigned to me. I reserve the right to revise my opinions in light of my ongoing review of materials, including data, documents, and depositions or other testimony that may subsequently come to light.

III. Summary of Opinions

10. Plaintiffs' experts have failed to establish that manufacturer Defendants in general or Purdue in particular engaged in misconduct that contributed to the opioid crisis in the Plaintiff Counties. The methodologies they employ violate basic scientific principles and fall well short of the standards required of published, peer-reviewed economic research, including the methods they themselves use in their academic work. These flawed methodologies produce inflated and unreliable estimates of the impact of Defendants' alleged misconduct, as well as damages, public nuisance costs, and abatement costs.

11. Professor Rosenthal purports to identify the causal impact of manufacturer Defendants' alleged misconduct on shipments of prescription opioids yet she fails to identify, let alone quantify, this alleged misconduct. Her methodology assumes, without any proof, that all of Defendants' marketing to physicians since 1995 was unlawful—despite the fact that this marketing concerns prescription drugs and is therefore regulated by the Food and Drug Administration ("FDA"). Her methodology also consists of building nonsensical models that

produce nonsensical results about how effective Defendants' marketing was—her estimates are many times larger than both the estimates found in the economics literature and Purdue's own assessment of the effectiveness of its marketing. Her "direct" model—the one Professor Cutler mainly relies on—is constructed in such a way that when applied to data completely unrelated to opioid sales, such as rain precipitation in Ohio or wins by Ohio professional sports teams wins, it shows that these "placebos" appear to have a large and statistically significant association with nationwide opioid sales, similar to the results from which Professor Rosenthal draws the incorrect inference that there was a large causal impact of promotion on sales. Professor Rosenthal's "indirect" model produces even more implausibly large estimates of the impact of Defendants' marketing and also relies on a methodology that has been discredited in the economics literature. Lastly, Professor Rosenthal purports to disprove the role of under-treated pain in explaining the rise of opioid sales since the mid-1990s. Yet her opinion rests on the assumption that there is no clinically justifiable use of opioids for chronic pain. This is contradicted by FDA-approved drug labels, the Centers for Disease Control and Prevention ("CDC") guideline on chronic pain treatment (the "CDC 2016 Guideline"), continued reimbursement of opioid prescriptions for chronic pain by public and private entities (including Plaintiffs), and opinions of practicing physicians.

12. Professor Cutler ignores the flaws in Professor Rosenthal's methodology and incorporates her flawed estimates into his own flawed methodology for estimating the impact of Defendants' alleged misconduct on opioid-related harms in the Plaintiff Counties. Professor Cutler's methodology substantially inflates the relationship between prescription opioid shipments and opioid-related mortality as Professor Cutler, like Professor Rosenthal, ignores the fundamental principle that correlation is not causation. He fails to consider, let alone rule out, that there are other factors that affect both opioid shipments and mortality and that could be the underlying cause for some or all of the observed relationship between opioid shipments and mortality. Such factors exist, as Professor Cutler has previously acknowledged in his own academic writings. They include a rise in social pain, distress, and dysfunction that has manifested itself in a rise in suicides, alcohol-related deaths, and drug poisonings. These deaths, termed "deaths of despair" in the economics literature, include deaths that do not involve any opioids and whose rise has coincided with the development of the opioid crisis. Similarly,

Professor Cutler fails to account for changes in the supply conditions of the illicit opioid market that are unrelated to either prescription opioid shipments or the demographic and economic characteristics included in his model. These include decreases in the prices of illicit opioids and increases in their availability and potency, especially following the surge in fentanyl use. He then applies his inflated measures of the relationship between prescription opioid shipments and mortality to other harms such as crime. This produces even more inflated estimates of the purported impact of prescription opioid shipments—for at least one of these other harms, there is no detectable association, let alone a causal relationship, once one accounts for the broader social factors captured by non-opioid-related "deaths of despair."

13. Professor McGuire ignores the flaws in both Professor Rosenthal's and Professor Cutler's methodologies and incorporates their flawed estimates into his own flawed methodology for estimating damages to the Plaintiffs and public nuisance costs to the Plaintiff Counties. For calculating damages, Professor McGuire simply translates Professor Rosenthal's and Professor Cutler's flawed findings into dollar amounts while also relying on a number of assumptions about the Plaintiffs' financial resources—assumptions that are either unproven or inconsistent with some of Plaintiffs' own fact witnesses. He also fails to properly evaluate the counterfactual world. To establish that there was a significant, unreasonable, and known or knowable public nuisance, Professor McGuire relies on Professor Cutler's flawed methodology and estimates for the alleged impact of prescription opioid shipments on harms; on Professor Rosenthal's flawed definition of clinically justifiable uses of opioids and his own flawed assessment of prescription opioid benefits versus costs; and on unsupported assumptions as to what Defendants knew or should have known. Each flawed input calls into question the reliability of Professor McGuire's final opinion that there was in fact public nuisance. Setting this aside, his quantification of the resulting costs is inflated given that he uses inflated inputs, overestimates the number of harms, and double counts certain costs.

14. Lastly, Professor Liebman and Dr. Alexander each present a 10+ year plan consisting of a multitude of programs that would purportedly abate the opioid crisis and whose associated costs are purportedly the responsibility of Defendants. Both of their analyses are fundamentally flawed because they fail to isolate the additional abatement costs that would be required due to Defendants' alleged misconduct. Instead, Professor Liebman's largest abatement programs

include treating individuals for substance abuse even though some of these individuals never used any prescription opioids, let alone any of Defendants' products. Similarly, he includes costs for programs that seek to prevent abuse of non-opioid and even non-drug substances such as alcohol and tobacco, as well as prevention programs that cover even broader topics such as violence and self-esteem. Dr. Alexander's abatement plan is flawed on an even more fundamental level. It is a national plan whose only tenuous link to the characteristics and future treatment needs of the Plaintiff Counties is these Counties' 2017 share of national opioid overdoses. This inappropriate, *ad hoc* pro-rating of national costs produces nonsensical results. Beyond these flaws, Professor Liebman's and Dr. Alexander's cost estimates, stretching a decade or more into the future, are both unreliable. The cost methodologies of both Professor Liebman and Dr. Alexander are predicated on assumptions that are unverifiable or undermined by available data, and they are often inconsistent with each other.

IV. Review of Professor Rosenthal's Analysis and Opinions

15. Professor Rosenthal's assignment broadly was to assess the causal impact of manufacturer Defendants' promotion of prescription opioids on use of prescription opioids in the Plaintiff Counties.[2] In order to conduct this assessment, Professor Rosenthal first reviews academic literature and other empirical research that attempts to measure the relationship between the marketing of prescription drugs and their sales. She then purports to quantify the impact of Defendants' allegedly unlawful marketing (which she considers to be all of Defendants' marketing) of prescription opioids on prescription opioid sales.[3] Finally, she claims to evaluate whether the growth in prescription opioid sales after 1995 can be explained by pain being under-treated prior to that time. As discussed below, Professor Rosenthal's analyses are deeply flawed. As a result, her opinions regarding the impact of manufacturer Defendants' promotion of prescription opioids on use of prescription opioids in the Plaintiff Counties are incorrect.

[2] Rosenthal Report, ¶ 8.
[3] Rosenthal Report, ¶¶ 11, 75.

A. Review of Professor Rosenthal's Estimates of the Impact of Manufacturer Defendants' Marketing on Opioid Shipments

16. In her report, Professor Rosenthal presents two models for purportedly quantifying the impact of Defendants' marketing on opioid sales, a "direct" model and an "indirect" model. Based on these models, Professor Rosenthal claims that she "can reasonably identify approximately 45-67% of [opioid morphine milligram equivalents] during the period of [her] analysis as caused by unlawful promotion."[4]

17. Professor Rosenthal's models are aggregate in nature. That is, she aggregates sales representatives' visits to physicians and other providers (known as sales visits or detailing visits)[5] and prescription opioid sales or shipments across opioid manufacturers and estimates the relationship between these aggregate measures over time. She does not attempt to measure whether the impact of sales visits differs depending on the product being marketed. Nor does she distinguish between sales visits for immediate-release versus extended-release products, combination versus single-ingredient products, products with abuse-deterrent versus non-abuse-deterrent formulations, or products containing different types of opioids.[6] She also does not distinguish between different marketing messages, or between marketing focused on the benefits of one opioid product over another versus marketing focused on the benefits and risks of opioids generally relative to non-opioid treatment options. She does not attempt to determine if the impact of a sales visit depends on how much the sales representative has met with the prescriber in the past or if it depends on whether sales representatives from competing companies are also visiting the prescriber. Nor does she assess whether marketing has a different impact depending on the specialty of the prescriber, the size of the prescriber's practice, the characteristics of the patient population the prescriber serves, or the prescriber's experience with the therapy over the

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[4] Rosenthal Report, ¶ 11.

[5] Professor Rosenthal ignores all other types of marketing other than sales visits to physicians and other providers. *See* Rosenthal Report, ¶ 56.

[6] Immediate-release opioids account for the vast majority (91 percent) of opioid prescriptions dispensed in Ohio since 2006 (the start of the damages period used by Plaintiffs' experts at the direction of counsel) (McGuire Damages Report, ¶ 7). Abuse-deterrent formulations, which include OxyContin's 2010 reformulation, account for 2 percent of all opioid prescriptions dispensed in Ohio since 2010. Hydrocodone products, which have been on the market for over 75 years, and largely consist of generic immediate-release combination products, account for 43 percent of opioid prescriptions dispensed in Ohio since 2006, and oxycodone products (also largely immediate-release products) account for 26 percent of opioid prescriptions dispensed in Ohio during this period. All of these statistics are based on the IQVIA Xponent data produced in this matter, which extend through April 2018.

almost quarter century she analyzes. Instead she assumes, without supporting evidence and in contradiction to prior research,[7] that the impact of all sales visits occurring at any given point in time is the same for all prescribers. As discussed in further detail below, the aggregate models that Professor Rosenthal uses are fundamentally flawed and contrary to the approach typically used in the academic literature.

1. Allegedly Unlawful Marketing

18. A key assumption underlying both of Professor Rosenthal's models, made at the instruction of counsel, is that "all or virtually all promotion by the manufacturer Defendants from 1995 to the present was unlawful."[8] Professor Rosenthal does not offer any support for this assumption nor conduct an assessment of its accuracy. I also am not aware of any other Plaintiffs' expert who has conducted a quantitative assessment of what proportion of Defendants' promotional efforts was deceptive.

19. As acknowledged by Professor Rosenthal, the FDA oversees both the approval and marketing of all prescription drugs, including prescription opioids, in the U.S.[9] Before any prescription drug can be sold legally in the U.S., it is subject to the FDA's approval process.[10] Once approved, pharmaceutical companies are allowed to market their drugs. FDA regulations require that promotional materials cannot be false or misleading, must reveal material facts about the product, and should present information about efficacy and risk in a balanced manner.[11] As a result, pharmaceutical marketing has a significant educational component. No regulations govern or constrain the size of a drug manufacturer's marketing efforts. Purdue's marketing expenditures for OxyContin as a percentage of sales since launch (1996 through 2017) were

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[7] Natalie Mizik and Robert Jacobson, "Are Physicians 'Easy Marks'? Quantifying the Effects of Detailing and Sampling on New Prescriptions," *Management Science* 50, no. 12, 2004, pp. 1704–1715; Dhaval Dave and Henry Saffer, "Demand for Smokeless Tobacco: Role of Advertising," *Journal of Health Economics* 32, no. 4, 2013, pp. 682–697; Pradeep K. Chintagunta et al., "Information, Learning, and Drug Diffusion: The Case of Cox-2 Inhibitors," *Quantitative Marketing and Economics* 7, no. 4, 2009, pp. 399–443.

[8] Rosenthal Report, ¶ 75.

[9] Rosenthal Report, ¶¶ 18–22.

[10] "FDA's Drug Review Process: Continued," FDA, https://www.fda.gov/drugs/drug-information-consumers/fdas-drug-review-process-continued, accessed May 6, 2019.

[11] "Guidance for Industry: Presenting Risk Information in Prescription Drug and Medical Device Promotion," U.S. Department of Health and Human Services et al. Draft Guidance, May 2009, pp. 3–4; 21 U.S.C. §§ 352(a), (n), (q)(1); 21 C.F.R. § 202.1(e)(5).

around 10 percent—below the 11–15 percent average estimated in the academic literature for the pharmaceutical industry as a whole.[12]

20. In addition to the initial approval for marketing a pharmaceutical product, the FDA has the ability to require subsequent label changes and continues to monitor the marketing materials disseminated by drug manufacturers post approval. The assumption that all Defendants' marketing was unlawful is inconsistent with the lack of enforcement actions taken by the FDA with respect to the vast majority of Defendants' marketing. For example, in connection with OxyContin's launch in January 1996, Purdue submitted to the FDA proposed promotional launch materials for OxyContin, including a journal advertisement, wholesaler and pharmacy sell sheets, and a titration guidelines card, among others. The FDA reviewed these materials, requested some modifications, and after some back-and-forth discussions with Purdue, approved the revised materials several months later.[13] A number of years later, in December 2002, the FDA sent Purdue a Warning Letter regarding two journal advertisements that the FDA determined either omitted or minimized OxyContin's safety risks. Purdue published corrective advertisements in the same journal the following month.[14] Since then, the FDA has not sent Purdue any other Warning Letters regarding its marketing.

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[12] Purdue Presentation, "Budget Presentation: Marketing & Sales Department," 1998, PDD1701024118–573 at 192; Purdue Presentation, "Budget Presentation: Marketing & Sales Department," 1999, PDD1701883704–4112; Purdue Presentation, "Budget Presentation: Marketing & Sales Department," 2000, PDD1701076902–7164; Purdue Budget Plan, "OxyContin® Tablets," 2001, PDD1715031061–114; Purdue Budget Plan, "OxyContin® Tablets," 2002, PDD1501030328–85; Purdue Presentation, "2004 Financial Year-in-Review: 2005 Budget Proposal," November 1, 2004, PPLPC20000042737; Purdue Presentation, "2009 Marketing Plan: OxyContin®," September 3, 2008, PPL003421761–918; Purdue Presentation, "2010 OxyContin® Tablets Budget Presentation," November 2009, PPLP003421085–114 at 110; Purdue Budget Proposal, "2011 OxyContin® Tablets Budget Submission," November 2010, PPLP003421115–98; Purdue Presentation, "2012 Budget Presentations: Marketing Overview," 2011, PPLP003421199–276; Purdue Marketing Plan, "2013 OxyContin® (oxycodone HCL controlled-release) Tablets Annual Marketing Plan," October 6, 2013, PPLP003420538–71; Purdue Presentation, "OxyContin 2015 Commercial Strategy Plan: Executive Committee Presentation," September 9, 2014, PPLP003420730–89; Purdue Presentation, "OxyContin 2016 Strategy Plan," May 5, 2015, PPLP003420790–812; Purdue Budget Proposal, "2018 Budget Proposal Sales and Promotion," October 12, 2017, PPLPC016000321828–66; Julie M. Donohue, "A Decade of Direct-to-Consumer Advertising of Prescription Drugs," T*he New England Journal of Medicine* 357, no. 7, 2007, pp. 673–681 at p. 673; Meredith B. Rosenthal et al., "Promotion of Prescription Drugs to Consumers," *The New England Journal of Medicine* 346, 2002, pp. 498–505; Rachel Kornfield et al., "Promotion of Prescription Drugs to Consumers and Providers, 2001–2010," *PLoS ONE* 8.3, 2013, e55504.

[13] Correspondence between Purdue and the FDA, January 11, 1996 to April 16, 1996, PPLP000614633–939.

[14] Letter from FDA to Purdue, "RE: NDA 20-553 OxyContin® (oxycodone HCI controlled-release) Tablets MACMIS ID# 11400: Warning Letter," December 24, 2002, PDD8013020701–10 at 02; Purdue Notice to Healthcare Practitioners, "Important Correction of Drug Information: OxyContin®," January 2003, PDD8013144610–1; FDA Warning Letter to Purdue, December 24, 2002, PDD8013020701–10; Important

21. To the extent Professor Rosenthal's assumption that all of Defendants' marketing was unlawful is premised on a belief that it was inappropriate for Defendants to market opioids for chronic pain, this ignores that the use of opioids for chronic pain was and is consistent with the FDA approved labels for many prescription opioids, including OxyContin.[15] In fact, the FDA has resisted calls to restrict the use of opioids in non-cancer chronic pain patients, let alone remove non-cancer chronic pain as an approved use entirely. In 2013, the FDA responded to Physicians for Responsible Opioid Prescribing, which had petitioned the FDA requesting it to "'[s]trike the term 'moderate' from the indication […] for non-cancer pain,'" "'[a]dd a maximum daily dose, equivalent to 100 milligrams of morphine for non-cancer pain,'" and "'[a]dd a maximum duration of 90-days for continuous [daily] use' for non-cancer pain'."[16] In its letter, the FDA indicated it would modify the labeling language for all extended-release long acting opioids from an indication focusing on "moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time" to an indication focusing on pain "severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate."[17] This change was implemented for the OxyContin label in 2014.[18] The FDA did not implement the other requested changes, instead

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Correction, January 2003, PDD8013144610. After receiving the Warning Letter, Purdue met with the FDA to request clarification on the letter and the FDA's guidelines regarding journal advertisements. As a result of that meeting and subsequent correspondence, the FDA made some changes to its Warning Letter and reissued it on January 17, 2003. *See* Letter from Kleinfeld, Kaplan and Becker, LLP to FDA, "RE: OxyContin® Professional Advertising," January 14, 2003, PDD1706207025–39; Letter from Kleinfeld, Kaplan and Becker, LLP to FDA, "RE: OxyContin® Professional Advertising," January 29, 2003, PKY181434547–61.

[15] The FDA-approved OxyContin label has mentioned use of OxyContin or opioids more generally for chronic pain throughout OxyContin's time on the market. For example, the 1996 label stated in the "Precautions" section "Physicians should individualize treatment in every case, using non-opioid analgesics, prn opioids and/or combination products, and chronic opioid therapy with drugs such as OxyContin in a progressive plan of pain management…." The "Maintenance of Therapy" section of the 2001 label stated "During chronic therapy, especially for non-cancer pain syndromes, the continued need for around-the-clock opioid therapy should be reassessed periodically (*e.g.*, every 6 to 12 months) as appropriate." Similar language is still included in OxyContin's label. The 2012 label includes the following language in the black box warning, "Proper dosing and titration are essential and OxyContin should be prescribed only by healthcare professionals who are knowledgeable in the use of potent opioids for the management of chronic pain." Similar language is included in the "Dosage and Administration" section of later labels. *See* FDA OxyContin Label, 1996, PDD1501603661−69, at 65; FDA OxyContin Package Insert, 2001, and FDA OxyContin Label, 2012, PPLPC031000946522−51, at 24.

[16] Letter from FDA to Physicians for Responsible Opioid Prescribing, "Re: Docket No. FDA-2012-P-0818," September 10, 2013, p. 1.

[17] Letter from FDA to Physicians for Responsible Opioid Prescribing, "Re: Docket No. FDA-2012-P-0818," September 10, 2013, p. 1.

[18] FDA OxyContin Label, April 2014, PPLP003275296–307, at 296.

noting that many professional organizations, including the American Medical Association and the American Society of Anesthesiologists "did not support the Petition" due in part to a "concern" that the changes "were not supported by scientific evidence" and that a "'one-size-fits-all' approach to maximum dose or duration of treatment would be problematic and inconsistent with the need for individualized treatment and the variability among patient responses to opioids."[19]

22. The assumption that all Defendants' marketing was unlawful also ignores Purdue's efforts since the early 2000s to make prescribers aware of the risks of OxyContin and disseminate accurate information about these risks. For example, in 2001 the FDA and Purdue collaborated on developing and implementing a risk management program ("RMP") to help detect and prevent misuse and abuse of OxyContin.[20] The plan required Purdue to train Purdue's sales force on OxyContin's revised label (which starting in 2001 included a black box warning related to OxyContin's misuse and overdose risks[21]), conduct comprehensive education programs for healthcare professionals, and develop a database for identifying and monitoring abuse and diversion of OxyContin.[22] Purdue's annual marketing and sales plans included drug abuse and diversion educational programs to help educate healthcare professionals, teenagers, parents, law enforcement officers, and discussion leaders about the dangers of prescription drug abuse.[23]

23. Such efforts were given an even greater impetus when Purdue entered into a Corporate Integrity Agreement ("CIA") with the Office of Inspector General ("OIG") as part of its 2007 plea agreement with the U.S. government. Professor Rosenthal herself notes the 2007 plea agreement,[24] but fails to note the establishment of the CIA or any other concrete actions Purdue

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[19] Letter from FDA to Physicians for Responsible Opioid Prescribing, "Re: Docket No. FDA-2012-P-0818," September 10, 2013, p. 5.
[20] "Prescription Drugs: OxyContin Abuse and Diversion and Efforts to Address the Problem," United States General Accounting Office Report to Congressional Requesters, No. GAO-04-110, December 2003.
[21] OxyContin's original label also warned of the dangers of misusing or abusing the drug. *See* Schedule II warning on FDA OxyContin Package Insert, July 1996, PDD1501603661–69 at 62.
[22] "Prescription Drugs: OxyContin Abuse and Diversion and Efforts to Address the Problem," United States General Accounting Office Report to Congressional Requesters, No. GAO-04-110, December 2003, p. 39.
[23] "Prescription Drugs: OxyContin Abuse and Diversion and Efforts to Address the Problem," United States General Accounting Office Report to Congressional Requesters, No. GAO-04-110, December 2003, p. 40; *see also* Deposition of J. David Haddox, February 8, 2019, 382:18–383:18, 427:16–21; Letter from King & Spalding to United States General Accounting Office, "Responses to Questions on the '100 County' Program," May 7, 2002, PKY183300102–8 at 5–7.
[24] Rosenthal Report, ¶ 47.

undertook in the years since it was established. These include, among others, the expansion of Purdue's previously instituted Promotion Monitoring Program (the program through which district managers evaluate and monitor sales representatives' interactions with physicians), the institution of review by the Compliance Officer of any issues flagged by this program, and the establishment of an ethics compliance hotline where Purdue employees can report anonymously any potential violations they have observed in the company. As part of the CIA, Purdue also committed to ongoing compliance training for all of its employees, subcontractors, and agents, as well as the engagement of independent reviewers who would periodically conduct reviews of Purdue's promotional and product services and the results of all such audits would be made available to the OIG upon its request.[25] In addition to these reports by independent reviewers, Purdue was obligated to provide an annual report to the OIG, and in turn the OIG had the right to conduct on-site reviews and examine Purdue's records, including the results of its Promotion Monitoring Program, to confirm the company's ongoing compliance with the CIA.[26]

24. In 2010, Purdue received FDA approval for a Risk Evaluation and Mitigation Strategies ("REMS") Program for OxyContin that Purdue developed as a successor program to the earlier OxyContin RMP.[27] The REMS Program included an educational program for prescribers which provided information on a number of topics such as proper patient selection, how to identify patients who are at risk for addiction, and information on potential abuse, misuse, overdose, and addiction from exposure to opioids.[28] In order to inform prescribers of the new REMS program, Purdue issued a "Dear Healthcare Professional" letter to physicians informing them of the OxyContin REMS educational program, sent out approximately 300,000 mailings to physicians and pharmacists, and budgeted over $550,000 from 2010 to 2011 for other programs designed to

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[25] Statement of United States Attorney John Brownlee on the Guilty Plea of the Purdue Frederick Company and its Executives for Illegally Misbranding Oxycontin, *U.S. v. The Purdue Frederick Company, Inc. et al.*, May 10, 2007, p. 4; Corporate Integrity Agreement between the Office of Inspector General of the Department of Health and Human Services and Purdue Pharma L.P., May 7, 2007, pp. 4–24.

[26] Corporate Integrity Agreement between the Office of Inspector General of the Department of Health and Human Services and Purdue Pharma L.P., May 7, 2007, pp. 27–31.

[27] Letter from FDA to Purdue, "NDA 022272," April 5, 2010, PPLP000141357–441. In 2012, this OxyContin-specific REMS program became incorporated into a single, shared FDA-approved REMS system for all extended-release long acting opioid products. *See* "Approved Risk Evaluation and Mitigation Strategies (REMS)," FDA, https://www.accessdata.fda.gov/scripts/cder/rems/, accessed May 6, 2019.

[28] Center for Drug Evaluation and Research, Approval Package for Application no. NDA 22-272, April 5, 2010, p. 5.

provide an overview of the REMS program to medical professionals.[29] Furthermore, when in 2012 the FDA approved a single, shared REMS system for all extended-release long acting opioid products on the market, Purdue's OxyContin, MS Contin, and Butrans all joined.[30]

25. Similarly, upon receiving FDA approval for a reformulated version of OxyContin in 2010, Purdue issued another "Dear Healthcare Professional" letter to physicians to inform them of the reformulated product. In this letter, Purdue cautioned prescribers that while it reformulated OxyContin "in an effort to make the tablet more difficult to manipulate for the purpose of intentional misuse and abuse, […] there is no evidence that the reformulation of OxyContin is less subject to misuse, abuse, diversion, overdose, or addiction."[31]

26. The actions of both Purdue and the FDA invalidate any assumption that "all or virtually all" of manufacturer Defendants' marketing since 1995 has been unlawful. Because Professor Rosenthal has not identified which of manufacturer Defendants' marketing was allegedly unlawful, her estimates do not constitute a measure of the impact of Defendants' alleged misconduct. Setting aside all the other issues in her methodology discussed below, Professor Rosenthal at best measures the impact of all of Defendants' detailing of physicians on opioid shipments, without any attempt to identify, let alone quantify or otherwise prove based on evidence, which of this detailing was allegedly unlawful.[32]

2. Factors Other Than Marketing That Drive Opioid Prescriptions

27. Professor Rosenthal does not account for factors other than detailing and price that might have affected opioid prescriptions during the relevant period. These factors include (but are not

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[29] "Risk Assessment and Risk Mitigation Reviews," Center for Drug Evaluation and Research, Application No. 22-272, undated, p. 6; Purdue Budget Proposal, "2011 OxyContin® Tablets Budget Submission," November 2010, PPLP003421115–98 at 29; Purdue Presentation, "OxyContin 2010 Incremental eMarketing Plan," July 23, 2010, PPLPC021000308007, slides 3–5; Purdue Presentation, "2011 OxyContin eMarketing Plan," August 23, 2010, PPLPC022000359032, slide 2; "Dear Healthcare Professional" Letter, December 2, 2008, PDD8901578397-98.

[30] Immediate-release products were not subject to a REMS until September 18, 2018. *See* "Approved Risk Evaluation and Mitigation Strategies (REMS)," FDA, https://www.accessdata fda.gov/scripts/cder/rems/, accessed May 6, 2019.

[31] Purdue Notice to Healthcare Practitioners, October 4, 2010, PPLPC031000685835–38 (emphasis in original).

[32] Professor Rosenthal claims that her model can be adjusted to "reflect other assumptions about the fact finder's conclusions" regarding which detailing was unlawful. See Rosenthal Report, ¶ 75. Any such adjustments cannot address the fundamental flaws in Professor Rosenthal's model, which I discuss in further detail in the sections that follow.

limited to): the role of third party payors (both government and private) in encouraging the use of opioids instead of alternative pain management treatments; the evolving professional consensus in medicine starting in the 1980s that led to greater attention to pain, as well as increased efforts to treat pain, including with opioid therapy; the growth of patient satisfaction surveys; and the general upward trend in medication use during this period.

28. In the 1980s (and perhaps even earlier) medical professionals began to raise concerns that pain was not being adequately treated.[33] In 1995, in response to a number of calls for improvement in pain assessment and treatment, the American Pain Society proposed adding pain as a fifth vital sign to be regularly assessed along with pulse, breathing, temperature, and blood pressure.[34] Notably, this proposal was made before the launch of OxyContin. In 1999, the Veterans Health Administration adopted the idea, and in 2000 it created a pain scale by which patients could inform doctors of their pain so that unrelieved pain could be identified and treated.[35] The Joint Commission (formerly the Joint Commission on the Accreditation of Healthcare Organizations) followed suit by adopting standards that specified the systematic use of a numeric pain scale when treating patients in 2001.[36] Similarly, the Federation of State Medical Boards published "Model Guidelines for the Use of Controlled Substances in the Treatment of Pain" in 1998 and expanded it to a model policy in 2004.[37] Both sets of guidelines advanced the belief that pain management is a key component of medical care and that opioid analgesics may be necessary for pain relief.[38] In 2011, the National Institute of Medicine argued

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[33] "Prescription Drugs: OxyContin Abuse and Diversion and Efforts to Address the Problem," United States General Accounting Office Report to Congressional Requesters, No. GAO-04-1103, December 2003, p. 1; *see also* Richard M. Marks and Edward J. Sachar, "Undertreatment of Medical Inpatients with Narcotic Analgesics," *Annals of Internal Medicine* 78, no. 2, 1973, pp. 173–81; Morgan, John P., "American Opiophobia: Customary Underutilization of Opioid Analgesics," *Controversies in Alcoholism and Substance Abuse*, 1986, 5(2): 163–73.

[34] James N. Campbell, "APS 1995 Presidential Address," *Pain Forum* 5, no. 1, 1996, pp. 85–88; Mitchell B. Max, "Improving Outcomes of Analgesic Treatment: Is Education Enough?," *Annals of Internal Medicine* 113, no. 11, 1990, pp. 885–89; "Pain: Current Understanding of Assessment, Management, and Treatments," National Pharmaceutical Council, Inc. and Joint Commission on Accreditation of Healthcare Organizations Report, December 2001, p. 29; David W. Baker, "The Joint Commission's Pain Standards: Origins and Evolution," The Joint Commission Report, May 5, 2017.

[35] "Pain as the 5th Vital Sign Toolkit," Department of Veterans Affairs Report, October 2000, pp. 13–14.

[36] David W. Baker, "The Joint Commission's Pain Standards: Origins and Evolution," The Joint Commission Report, May 5, 2017, pp. 3–4.

[37] Federation of State Medical Boards of the United States, Inc. "Model Policy for the Use of Controlled Substances for the Treatment of Pain," *Journal of Pain and Palliative Care Pharmacotherapy* 19, no. 2, 2005, p. 73.

[38] Federation of State Medical Boards of the United States, Inc. "Model Policy for the Use of Controlled Substances for the Treatment of Pain," *Journal of Pain and Palliative Care Pharmacotherapy* 19, no. 2, 2005, p. 73.

that pain management, in which opioids can serve a "safe and effective" role, is "a moral imperative, a professional responsibility, and the duty of people in the healing professions."[39] It is likely, therefore, that opioid use increased in the 1990s and 2000s at least in part due to the general increased attention from the medical community on better pain treatment as evidenced by the guidelines described above.

29. Over the time period in question, there was also increasing use of patient satisfaction surveys to assess hospital and/or provider quality.[40] Of particular note, in 2006, the Centers for Medicare and Medicaid Services ("CMS") introduced the Hospital Consumer Assessment of Healthcare Providers and Systems ("HCAHPS") survey. This survey is offered to patients after they are discharged from hospitals and its results are disseminated publicly. This allows healthcare consumers to make decisions based on these results, and under the Affordable Care Act, hospitals also receive Medicare payments based in part on survey results.[41] Until recently, one of the survey's questions asked, "How often did the hospital or provider do everything in their power to control your pain?"[42] Such surveys can encourage prescribing of pain medications to the extent that such prescribing increases patient satisfaction scores. Indeed, treatment with opioids has been found to positively contribute to patient satisfaction ratings.[43] As a result, doctors conscious of the HCAHPS survey, as well as other patient satisfaction surveys that ask about treatment of pain, may have become more likely to prescribe opioids to their patients in order to receive better scores.[44]

30. The structure of healthcare reimbursement systems can also have a substantial influence on the treatment options chosen by providers and consumers. In the 1970s, multidisciplinary

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[39] Institute of Medicine, Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research (Washington, DC: The National Academies Press, 2011), p. 3.
[40] *See, e.g.*, Eyal Zimlichman et al., "The Road to Patient Experience of Care Measurement: Lessons from the United States," *Israel Journal of Health Policy Research* 2, no. 35, 2013, pp. 1–6.
[41] "Patient Satisfaction Surveys," NEJM Catalyst, January 1, 2018, https://catalyst.nejm.org/patient-satisfaction-surveys/, accessed January 7, 2019.
[42] Jerome Adams et al., "Are Pain Management Questions in Patient Satisfaction Surveys Driving the Opioid Epidemic?," *American Journal of Public Health* 106, no. 6, 2016, pp. 985–86.
[43] Jessica Shill et al., "Factors Associated with High Levels of Patient Satisfaction with Pain Management," *Academic Emergency Medicine* 19, no. 10, 2012, pp. 1212–1215.
[44] Jerome Adams et al., "Are Pain Management Questions in Patient Satisfaction Surveys Driving the Opioid Epidemic?," *American Journal of Public Health* 106, no. 6, 2016, pp. 985–86.

pain treatment teams were common.[45] These teams traditionally consisted of a number of different providers such as physicians, pain psychologists, and physical therapists, all of whom were located in the same facility and provided a bundled package of services, primarily using a combination of cognitive and physical therapy.[46] However, a shift in reimbursement systems to the fee-for-service model in the 1980s and later the managed care model in the 1990s reduced the popularity of multidisciplinary teams.[47] The managed care model from the 1990s also placed an emphasis on cost saving and mandated that patients received each of their pain treatments at facilities identified as the most cost-effective for the specific treatment. This discouraged members of multidisciplinary teams from inhabiting the same facility and further discouraged the use of a multidisciplinary team approach towards pain management.[48] The managed care model also empowered third party payors such as health insurers and pharmacy benefit managers ("PBMs") to steer consumers towards cheaper treatment options within a therapeutic category through the use of formulary and utilization management techniques.[49] This aspect of the managed care model also incentivized physicians to prescribe and consumers to use drug therapies (including but not limited to opioids) as they were usually cheaper than many alternative treatments for patients needing pain therapy, including surgery or prolonged physical therapy or counseling.[50]

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[45] D. Andrews Tompkins et al., "Providing Chronic Pain Management in the 'Fifth Vital Sign' Era: Historical and Treatment Perspectives on a Modern-Day Medical Dilemma," *Drug and Alcohol Dependence* 173, no. 1, 2017, pp. 1–26 at pp. 4–6.

[46] D. Andrews Tompkins et al., "Providing Chronic Pain Management in the 'Fifth Vital Sign' Era: Historical and Treatment Perspectives on a Modern-Day Medical Dilemma," *Drug and Alcohol Dependence* 173, no. 1, 2017, pp. 1–26 at p. 4.

[47] D. Andrews Tompkins et al., "Providing Chronic Pain Management in the 'Fifth Vital Sign' Era: Historical and Treatment Perspectives on a Modern-Day Medical Dilemma," *Drug and Alcohol Dependence* 173, no. 1, 2017, pp. 1–26 at p. 5.

[48] D. Andrews Tompkins et al., "Providing Chronic Pain Management in the 'Fifth Vital Sign' Era: Historical and Treatment Perspectives on a Modern-Day Medical Dilemma," *Drug and Alcohol Dependence* 173, no. 1, 2017, pp. 1–26 at p. 5.

[49] Katie Thomas and Charles Ornstein, "Amid Opioid Crisis, Insurers Restrict Pricey, Less Addictive Painkillers," *The New York Times*, September 17, 2017, available at https://www.nytimes.com/2017/09/17/health/opioid-painkillers-insurance-companies html, accessed May 6, 2019; Harrison Jacobs, "Pain Doctors: Insurance Companies Won't Cover the Alternatives to Opioids," *Business Insider*, August 10, 2016, available at https://www.businessinsider.com/doctors-insurance-companies-policies-opioid-use-2016-6, accessed January 17, 2019.

[50] Katie Thomas and Charles Ornstein, "Amid Opioid Crisis, Insurers Restrict Pricey, Less Addictive Painkillers," *The New York Times*, September 17, 2017, available at https://www.nytimes.com/2017/09/17/health/opioid-painkillers-insurance-companies html, accessed May 6, 2019; D. Andrews Tompkins et al., "Providing Chronic Pain

31. Further, while formulary restrictions and utilization management for opioid products are increasingly becoming the norm,[51] they only became commonplace recently. A 2017 study of Medicare prescription drug plans from 2006 to 2015 found that about two thirds of opioids had no formulary restrictions in either 2006 or 2011 and about one third of opioids still had no restrictions as of 2015.[52] In some cases, even when utilization management techniques are in place, they have not facilitated a switch away from opioids to non-opioid alternatives. An even more recent study examined the 2017 prescription drug coverage policies for lower back pain treatments among 50 Medicaid, Medicare Advantage, and commercial insurance plans. The authors found that while utilization management techniques were common for opioid products, even in 2017, most opioid products remained on low formulary tiers with copayments as low as $10 or $15 per prescription.[53]

32. Professor Rosenthal also ignores the upward trend in the overall level of medication dispensing. According to data from the National Ambulatory Medical Care Survey ("NAMCS"), the total number of medications—including both prescription and non-prescription medications, immunizations, vitamins, and supplements—dispensed or prescribed during physician office visits in the U.S. has increased steadily since at least 1996. Between 1996 and 2011, the total number of medications dispensed or prescribed by physicians nationwide increased by 140 percent. Similar growth was observed when measured on a per capita basis—a 107 percent increase in the number of medications dispensed per capita.[54]

Management in the 'Fifth Vital Sign' Era: Historical and Treatment Perspectives on a Modern-Day Medical Dilemma," *Drug and Alcohol Dependence* 173, no. 1, 2017, pp. 1–26.

[51] Katie Thomas and Charles Ornstein, "Amid Opioid Crisis, Insurers Restrict Pricey, Less Addictive Painkillers," *The New York Times*, September 17, 2017, available at https://www.nytimes.com/2017/09/17/health/opioid-painkillers-insurance-companies html, accessed May 6, 2019.

[52] Elizabeth A. Samuels et al., "Medicare Formulary Coverage Restrictions for Prescription Opioids, 2006 to 2015," *Annals of Internal Medicine* 167, no. 12, 2017, pp. 895–96.

[53] Dora H. Lin et al., "Prescription Drug Coverage for Treatment of Low Back Pain Among US Medicaid, Medicare Advantage, and Commercial Insurers," *JAMA Network Open* 1, no. 2, 2018.

[54] NAMCS only collects information on a certain number of medications in each office visit. Because information for only six medications per visit was collected for 1996–2002, this analysis limits the medication count per visit to six for all years so as not to introduce artificial growth over time due to changes in the maximum medication count allowed. In other words, it assumes that all office visits involving six or more medications involved exactly six medications. As a result, the counts understate the total number of medications. The proportion of office visits involving six or more medications increased from three percent in 1996 to 17 percent in 2011, and peaked at 24 percent in 2015. Per capita values use national population estimates from Professor Rosenthal's Report, Table D (a).

33. It would have been possible for Professor Rosenthal to measure some of these other drivers of opioid prescriptions[55] and include them in her model as additional factors that potentially impact opioid sales, but she has made no meaningful attempt to do so.[56] This omission is particularly glaring given that in her deposition Professor Rosenthal testified that there are other factors, beyond marketing, which are important in explaining physician behavior and that "the question here is really what is the incremental impact of marketing on the prescriptions that physicians write."[57] Yet, she built a model which is incapable of answering this question. As discussed in more detail below, Professor Rosenthal's model only allows sales visits and prices to affect opioid sales. As a result, this flawed model predicts that without detailing to physicians between 1993 and 2018, there would have been virtually no sales of prescription opioids during this period; in fact, in several years, her model generates the nonsensical prediction of negative sales. I discuss in more detail the flaws of this model below.

3. Review of Professor Rosenthal's "Direct" Model

34. Professor Rosenthal's "direct" approach consists of estimating the relationship between an aggregate measure of Defendants' detailing of physicians and aggregate opioid sales at a

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[55] During his deposition, Plaintiffs' damages expert, Professor McGuire, acknowledged that there are a number of other factors apart from marketing by drug manufacturers that affect physician prescribing behavior. *See* Deposition of Thomas McGuire, April 30, 2019 ("McGuire April 30 Deposition"), 785:16–787:10 (identifying manufacturer marketing, overall cost to the patient, applicable formulary, applicable utilization management protocols, physician's experience with a particular medication, and physician's overall years of experience as factors that might affect physician prescribing).

[56] While Professor Rosenthal purports to account for certain (but not all) "key" events that she identifies as having "helped promote expanded opioid prescribing" and "subsequent public health and regulatory events" in version C of her direct model, she merely includes indicators for when these events occurred. Hence, in addition to failing to account for all events she herself considers "key," for the events that she does purport to account for, she fails to allow their impact to change over time. Further, Professor Rosenthal dismisses this version of her model because the impact she estimates from some of these events is "counterintuitive." Specifically, she finds that the rescheduling of hydrocodone products from Schedule III to Schedule II had a positive impact on overall opioid sales whereas it would be expected to have had a negative impact. Instead of questioning her overall modeling approach, Professor Rosenthal simply ignores this version of her model. Professor Rosenthal motivates this decision by stating that the five "key" events she included in the model do not have a jointly statistically significant impact on opioid sales. Yet more than a month after the filing of her report, Professor Rosenthal submitted an errata sheet that reveals that these five events were in fact jointly statistically significant. Rosenthal Report, ¶¶ 57, 73; Errata to Rosenthal Report, May 2, 2019, p. 2.

[57] Deposition of Meredith Rosenthal, May 4, 2019 ("Rosenthal Deposition"), 97:9–11.

national, monthly level while accounting for only one other factor—opioid prices.[58] There are numerous flaws in Professor Rosenthal's implementation of her approach and, as a result, the model does not even provide a valid estimate of the association between Defendants' detailing and opioid sales, let alone the causal impact.

35. Professor Rosenthal's analysis is founded on some fundamental methodological errors. First, almost all of the peer-reviewed academic literature on demand for pharmaceutical products—including Professor Rosenthal's own published research—uses an econometric model grounded in economic theory.[59] Restrictions imposed by economic theory "keep the modeler honest" by ensuring consistency with the underlying economic phenomenon—here, choices among alternative treatments for pain. Use of an *ad hoc* model divorced from any underlying structure, such as Professor Rosenthal's, is generally understood by economists to be an improper basis for assessing causal relationships or predicting counterfactual outcomes.

36. Second, Professor Rosenthal aggregates an entire category of products into a single time series measure of quantity sold (total opioid morphine milligram equivalents ("MMEs")), "explained" by a single time series measure of promotion (stock of total opioid detailing by all manufacturers) and a single time series measure of prices. Again, this is contrary to the normal approach in the academic literature, which generally models changes in demand of individual products within a category. Aggregation up to the category level conceals economically significant variation across products. For example, in this case, while some opioid products are branded drugs that are promoted by their manufacturers, a large part of total sales volume in this category consists of generic products that are not promoted. There has also been significant entry by new products and important changes in product characteristics. A serious effort to establish the causal impact of promotion on sales would respect these distinctions rather than

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[58] As discussed above, Professor Rosenthal's model C includes some indicator or "dummy" variables that she believes can account for certain "key" events.

[59] One widely used choice is the "logit demand system for differentiated products." *See, e.g.*, Simon P. Anderson and Andre de Palma, "The Logit as a Model of Product Differentiation," *Oxford Economic Papers* 44, no. 1, 1992, pp. 51–67; Steven T. Berry, "Estimating Discrete-Choice Models of Product Differentiation," *The RAND Journal of Economics* 25, no. 2, 1994, pp. 242–62; Andrew Ching and Masakazu Ishihara, "The Effects of Detailing on Prescribing Decisions under Quality Uncertainty," MPRA Paper No. 8324, 2008; Gregory S. Crawford and Matthew Shum, "Uncertainty and Learning in Pharmaceutical Demand," *Econometrica* 73, no. 4, 2005, pp. 1137–73; Pierre Azoulay, "Do Pharmaceutical Sales Respond to Scientific Evidence," *Journal of Economics & Management Strategy* 11, no. 4, 2002, pp. 551–94.

mask them and would follow the published literature in estimating a model based on data disaggregated to at least the product level.

37. Instead, Professor Rosenthal's "direct" approach amounts to curve-fitting a single aggregate measure of opioid sales in which, by manipulating the data on physician detailing, she is able to create an artificially strong association between such activity and opioid sales. To do so, she breaks the data into three sub-periods—January 1993–February 2002, March 2002–July 2010, and August 2010–May 2018—and estimates a different relationship between detailing visits and opioid sales within each sub-period. Professor Rosenthal claims to have identified the start and end date of each sub-period based on when the data indicated that the relationship between detailing visits and opioid sales changed. Professor Rosenthal accordingly chooses her model to ensure that detailing visits best "fit" the pattern of opioid sales.[60] In other words, Professor Rosenthal does not have an *a priori* theory as to why the relationship should change at these exact points in time or why there should be two breaks as opposed to one. Nor does she investigate if these "breaks" could be the result of a host of other factors that are omitted from her model that could affect both opioid sales and detailing visits.

38. That Professor Rosenthal manipulates the data is evident by the fact that she uses different methods of estimating the relationship across the three sub-periods. In particular, when estimating the relationship during the third sub-period, Professor Rosenthal inexplicably builds in a linear trend in this relationship—what she terms a "dummy trend" or a "secular decrease" in the relationship.[61] Professor Rosenthal offers no explanation for why she does this in the first place or why she does so only for the third sub-period but not the first or the second. The consequence of this modeling choice is clear, however—it enables Professor Rosenthal to claim that her model can explain over 99 percent of the variation over time in national opioid sales.[62]

39. The fact that her model can explain 99 percent of the variation in opioid sales despite not including important factors that likely drove opioid sales makes clear that her model is attributing sales to marketing that it should not. Instead of trying to estimate the true relationship

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[60] Rosenthal Report, ¶¶ 65, 68.
[61] Rosenthal Report, ¶ 71, Table 1.
[62] Rosenthal Report, ¶ 72. Econometricians generally do not place much weight on the fraction of variance explained as a measure of the validity of a model, focusing instead on consistency of results with theoretical predictions and other diagnostic tests.

between marketing and opioid sales, Professor Rosenthal has structured her measure of that relationship to ensure the largest possible association.[63]

40. The results of Professor Rosenthal's analysis thus reflect the way she has constructed her model, rather than any underlying economic relationship. Consider the following "placebo tests" that I conducted. Instead of detailing visits, I substitute into Professor Rosenthal's model several alternative data series that clearly have no economic relationship to national trends in opioid shipments to test whether her model would nevertheless find such a relationship. These data series are (1) monthly total rain precipitation in the U.S., (2) monthly rain precipitation in Ohio, and (3) monthly wins by two of Cleveland's professional sports teams, the Indians and the Cavaliers. Even though each of these data series is unrelated to opioid shipments, when I incorporate each series into Professor Rosenthal's model instead of the data she uses to measure promotion and apply the same process of "fitting" the model to the data that Professor Rosenthal uses, I generate very similar results to the ones Professor Rosenthal obtains for detailing visits.

41. Specifically, I find that rain precipitation across the U.S., rain precipitation in Ohio only, and wins by Cleveland's professional sports teams can each "explain" over 99 percent of the variation in nationwide opioid sales between 1993 and 2018. I also find that each of these series has a "significant" impact on opioid sales during each of the three "eras of the opioid market" that Professor Rosenthal identifies. Indeed, Professor Rosenthal's direct approach indicates that one inch of rain in Ohio during January 1996 caused more than 10.4 million opioid MMEs to be dispensed nationwide during that month, and by May 2018, that same inch of rain caused more than 6.4 billion opioid MMEs to be dispensed in total. Similarly, according to Professor

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[63] In her report, Professor Rosenthal also proceeds directly with applying her model results without doing any of the basic statistical tests, normally done prior to analyzing time series data, to confirm that the assumptions underlying her model are in fact satisfied. For instance, she does not test for serial correlation in her data, *i.e.*, whether the portion of opioid sales that remains unexplained by her model in one month is correlated with the unexplained portion of opioid sales in another month. Such a correlation violates a key assumption underlying the estimation of her model and calls into question Professor Rosenthal's conclusions about the precision and statistical significance of her estimates. A careful econometric analysis would test for such patterns and account for them using standard techniques such as adjusting the standard errors of the regression coefficients or including lagged values of the outcome variable as additional explanatory variables. *See* Jeffrey M. Wooldridge, *Introductory Econometrics: A Modern Approach*, Sixth Edition (Boston, MA: Cengage Learning, 2016), pp. 373–96. In her deposition, Professor Rosenthal testified that she has conducted such tests (though such tests were not included in her production) and found some evidence of serial correlation in the earlier period of her data. Yet there is no evidence that she performed any adjustments to her model to account for her findings of serial correlation. Rosenthal Deposition, 140:24–141:16.

Rosenthal's direct approach, one Cleveland Cavaliers win in January 1996 caused more than 3.1 million opioid MMEs to be dispensed nationally that month, and by May 2018, caused more than 2.0 billion opioid MMEs to be dispensed nationally in total.

42. The flaws in Professor Rosenthal's methodology are also illustrated by the nonsensical results it produces. In particular, Professor Rosenthal's model produces a *negative* depreciation rate for the stock of marketing.[64] In other words, Professor Rosenthal's model says that a sales representative's visit to a physician had a larger impact on opioid sales years and even decades after the visit occurred than it had immediately after the visit. This contradicts not only the findings of a large body of economics literature and Purdue's internal marketing studies, but also common sense. A negative depreciation rate implies that the influence, if any, of any given instance of promotion does not fade over time, but rather keeps increasing. Its impact on prescribing will be much larger in the future than its contemporaneous effect, and in Professor Rosenthal's model, the further in the past that a detailing visit took place, the larger its impact on current prescribing decisions. Yesterday's detailing visit is less impactful on today's prescribing decisions than a similar visit last week, which is less impactful than a similar visit last month, which in turn is even less impactful than one last year, and much less impactful than one a decade ago.

43. Professor Rosenthal attempts to explain the contradiction between her model's negative depreciation rate and the positive depreciation rate estimated in the economics literature on pharmaceutical marketing by claiming that this contradiction is due to opioids being different from other drugs as a result of their addictive properties.[65] Yet, she presents no evidence to support this claim, and the available evidence contradicts her claim. The economics literature on other addictive substances such as cigarettes has consistently estimated that the impact of marketing depreciates for these substances and does so at a fast rate. In fact, a number of studies have found that all or virtually all of the impact disappears within a year.[66]

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[64] Rosenthal Report, Table 1.

[65] Rosenthal Report, ¶ 72; Rosenthal Deposition, 249:12–250:1.

[66] *See, e.g.*, Dhaval Dave and Henry Saffer, "Demand for Smokeless Tobacco: Role of Advertising," *Journal of Health Economics* 32, no. 4, 2013, pp. 682–97; Barry J. Seldon and Roy Boyd, "The Stability of Cigarette Demand," *Applied Economics* 23, 1991, pp. 319–26 at p. 321; Badi H. Baltagi and Dan Levin, "Estimating Dynamic Demand for Cigarettes Using Panel Data: The Effects of Bootlegging, Taxation and Advertising Reconsidered," *The Review of Economics and Statistics* 68, no. 1, 1986, pp. 148–55 at p. 152.

44. There are also good reasons to expect that the effects of deceptive marketing, in particular, would have depreciated rapidly. For example, physicians could observe occurrences of dependence or addiction among their own and their colleagues' patients and adjust their prescribing accordingly, rather than blindly believing any supposedly deceptive claims from Defendants. Moreover, it strains belief that physicians would not have become even more aware of the potential for prescription opioid abuse over time as stories about this issue gained traction in the popular press, both in Ohio and nationally, starting in 2001.[67] Further, since the early 2000s, research on prescription opioid abuse started to appear frequently in peer-reviewed medical journals.[68] Information about the consequences of opioid prescribing would be expected to invalidate or "write off" a larger proportion of any built-up "stock" of promotion to the extent that promotion had fostered a belief that opioids were not addictive or unlikely to be abused.

45. To illustrate the nonsensical implications of a negative depreciation rate, consider the following. According to Professor Rosenthal's model, one sales representative's visit to a physician in January 1996 caused [redacted] opioid MMEs to be dispensed that month. A decade later, in January 2006, that same visit caused more than [redacted] as many opioid MMEs to be dispensed—[redacted] MMEs. Two decades later, the impact of that January 1996 visit was even larger, reaching [redacted] MMEs in January 2016. By May 2018, the end of Professor Rosenthal's data, that same January 1996 visit had purportedly caused [redacted] opioid MMEs to be dispensed nationwide. To put these MME quantities in perspective, [redacted] MMEs is equivalent to [redacted]

[67] A Factiva search among all publications in the U.S. public press written in English that contained the word "OxyContin" and either "abus," "misus," "addict," or "crisis" produced more than 1,000 publications annually between 2001 and 2010. When the search is limited to Ohio publications, there were dozens of publications each year starting in 2001 and more than 100 publications in 2010.

[68] A search of PubMed, an online depository of citations for biomedical literature maintained by the National Institutes of Health, for publications containing the words "OxyContin" or "oxycodone" and either "addiction," "abuse," "abusing," "abused," "abuser," "abusers," "misuse," "misusing," "misused," "addict," "opioid use disorder," or "crisis" produced at least a dozen publications each year starting in 2001 and more than 50 by 2010.

20 mg OxyContin pills (the most commonly dispensed OxyContin dose)[69] which is equivalent to more than [redacted] 30-day prescriptions at a dose of 40 mg per day.[70]

46. In contrast to Professor Rosenthal's results, a 2018 study of the marketing of an antipsychotic drug estimated that one detailing visit was associated with approximately 0.12 prescriptions in the month of the detailing visit and 0.3 prescriptions in total.[71] A 2004 study that analyzed more than two million prescriptions written by 74,000 physicians, and that Professor Rosenthal cited herself, estimated that on average, the overall number of new prescriptions associated with one detailing visit ranged from 0.2 to 1.6 prescriptions.[72] Purdue's estimates for the effectiveness of its opioid promotion are of similar magnitude. Purdue studies estimated that one detailing visit for OxyContin generated between 0.1 and 5 OxyContin prescriptions—nowhere near the estimates produced by Professor Rosenthal's model.[73]

47. Beyond these fundamental implementation flaws, Professor Rosenthal's direct model, even if implemented correctly, would measure only the association between Defendants' detailing and opioid shipments and could not be used to make any statements about a "causal" impact of Defendants' detailing. To suggest otherwise, as Professor Rosenthal does—"in economic terms there is a causal relationship between the Defendants' promotion and the

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[69] Throughout the period analyzed by Professor Rosenthal, a large majority [redacted] of (branded and generic) OxyContin prescriptions dispensed in the U.S. involved 40 mg or lower pill strengths and at least [redacted] percent involved 20 mg or lower strengths. IQVIA Xponent data for the period since 1999 reveal similar statistics for Ohio. In Ohio, at least 74 percent of (branded and generic) OxyContin prescriptions involved 40 mg or lower pill strengths and at least 40 percent involved 20 mg or lower pill strengths. Similarly, according to the claims data produced by Plaintiffs for beneficiaries covered under their health plans, just over two thirds (67 percent) of (branded or generic) OxyContin claims were for a daily dose of 80mg or less. Further, the majority (62 percent) of (branded or generic) OxyContin use episodes lasted 30 days or less, and more than two thirds (73 percent) lasted 90 days or less. For the purposes of this calculation, I limit my analysis to beneficiaries whose first (branded or generic) OxyContin prescription was filled in at least 60 days after the beneficiary's first medical or pharmacy claim in the data and at least 365 days prior to the last medical or pharmacy claims. I define an episode as continuous use of (branded or generic) OxyContin, allowing at most 60-day breaks where the break duration is based on the days supply for each prescription.

[70] The number of prescriptions is calculated by dividing [redacted] by 60 (the number of 20 mg pills in a 30-day, 40 mg per day prescription), *i.e.*, [redacted]

[71] Bradley T. Shapiro, "Informational Shocks, Off-Label Prescribing and the Effects of Physician Detailing," *Management Science* 64, no. 12, pp. 5925–45 at p. 5926.

[72] Natalie Mizik and Robert Jacobson, "Are Physicians 'Easy Marks'? Quantifying the Effects of Detailing and Sampling on New Prescriptions," *Management Science* 50, no. 12, 2004, pp. 1704–1715 at pp. 1704, 1714.

[73] Purdue Presentation, "OxyContin: Marketing Mix Modeling Result," July 2012, PPLP003409899–935 at 912–13; Purdue Presentation, "Oxycontin Marketing Mix," undated, PPLP003409951–94 at 68–73.

prescriptions of opioids"[74]—is incorrect. Indeed, it is contrary to the fundamentals of econometric analysis.

48. For any econometric analysis to be credible, the econometrician needs to first establish that she has a proper strategy of identifying a causal relationship rather than a mere association—simply establishing that two variables move together, as Professor Rosenthal claims she does, only fulfills the latter, but not the former goal. Indeed, two variables, X and Y, can be observed to move together not only because X causes Y but also because Y causes X. This is a well-known problem in economics—referred to as "simultaneous causality" or "simultaneity"—when "causality runs 'backward' as well as forward."[75] In the current context, this means that a company's marketing decisions may drive current and future sales, but current and anticipated sales may also drive marketing. When such simultaneity is present, a model like Professor Rosenthal's picks up both effects and generates an upwardly biased estimate of the impact of marketing on sales.

49. This bias is exacerbated when there is another variable, Z, that is omitted from the model despite being related to both X and Y. In this context, Z represents any of the factors discussed above in Section IV.A.2 that are omitted from Professor Rosenthal's model despite being important drivers of both opioid prescriptions and opioid manufacturers' marketing decisions. For instance, since at least the 1980s, the increased clinical emphasis on treating pain likely has driven both opioid sales and opioid drug manufacturers' marketing decisions. The omission of such factors is another well-known problem in economics—the problem of "omitted variable bias,"[76] which as the name indicates, is yet another reason why Professor Rosenthal's model generates a biased estimate of the impact of marketing on opioid sales.

50. Both of these are fundamental problems in econometric analysis that are discussed at length in introductory textbooks and described as the main threats to the validity of empirical

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[74] Rosenthal Report, ¶ 64.
[75] James H. Stock and Mark W. Watson, *Introduction to Econometrics*, Second Edition (Boston, MA: Pearson Education, Inc., 2007), p. 324.
[76] James H. Stock and Mark W. Watson, *Introduction to Econometrics*, Second Edition (Boston, MA: Pearson Education, Inc., 2007), p. 316.

analyses.[77] Their solutions are just as well known, with one of the most common involving the use of "instrumental" variables. These variables are used as "instruments" to remove the part of marketing that is a response to sales or driven by other factors that drive both sales and marketing. Thus, when proper instruments are identified and applied, they can help provide an estimate of the causal effect of marketing on sales.[78]

51. The problem and the solution are well known to Professor Rosenthal. In her own published research, Professor Rosenthal has both recognized the problem that marketing, and specifically physician detailing, is simultaneously determined with drug sales, and employed the solution of instrumental variables in an attempt to identify the causal impact of detailing.[79] Yet in her report, Professor Rosenthal fails to even acknowledge that a problem exists with her model, let alone attempt any solution. In her deposition, Professor Rosenthal even claimed that this problem only applies to models that examine the impact of marketing on a single drug product and does not affect aggregate models such as the one she put forward in this case.[80] This statement is glaringly false—it is contradicted by Professor Rosenthal's own academic research where she notes the problem, and applies the solution, to exactly the same type of aggregate model she is using in this case.[81] It is also contradicted by economic literature cited by Professor Rosenthal in her report as purported support for her findings.[82] It is also contradicted by Schmalensee's seminal work on the economics of advertising, which cautioned more than 45 years ago that aggregate models of the type used here by Professor Rosenthal are "likely to yield badly biased estimates" and "over-estimate the impact of advertising."[83] Professor Rosenthal's

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[77] James H. Stock and Mark W. Watson, *Introduction to Econometrics*, Second Edition (Boston, MA: Pearson Education, Inc., 2007), p. 316. Economists often refer to the consequences of simultaneous determination, reverse causality, or omitted variables with the catch-all term "endogeneity problems."

[78] James H. Stock and Mark W. Watson, *Introduction to Econometrics*, Second Edition (Boston, MA: Pearson Education, Inc., 2007), pp. 318, 325.

[79] Meredith B. Rosenthal et al., "Demand Effects of Recent Changes in Prescription Drug Promotion" in *Frontiers in Health Policy Research*, Number 6, eds. David M. Cutler and Alan M. Garber (Cambridge, MA: The MIT Press, 2003) ("Rosenthal et al. (2003)"), p. 15.

[80] Rosenthal Deposition, 354:8–356:6.

[81] Rosenthal et al. (2003), Table 1.3.

[82] Ernst R. Berndt et al., "Information, Marketing, and Pricing in the U.S. Antiulcer Drug Market," *The American Economic Review* 85, no. 2, 1995, pp. 100–05 at p. 103.

[83] Richard Schmalensee, *The Economics of Advertising*, (London: North-Holland Publishing Company, 1972), pp. 54, 116–19. Indeed, it is the vulnerability to simultaneity bias of poorly specified aggregate models such as the one Professor Rosenthal uses here, and the difficulty of addressing it satisfactorily using this type of data, that has led the literature towards product level models, or even finer levels of aggregation such as geographic units (*e.g.*, county-

assertion is also contradicted by common sense. If individual opioid manufacturers' marketing decisions respond to their own product sales (as Professor Rosenthal acknowledges[84]), then the sum of those marketing decisions will also be responsive to the sum of all opioid sales, thereby causing simultaneity bias in Professor Rosenthal's model. Professor Rosenthal's insistence that her model is somehow immune from this bias and provides an estimate of the "causal" impact of Defendants' detailing,[85] flies in the face of the literature, her own academic work, and common sense itself.

52. In sum, far from using a "fair, accurate and econometrially [sic] sound method"[86] to establish a causal relationship between Defendants' detailing of physicians and sales of prescription opioids, Professor Rosenthal's flawed use of an inappropriate econometric model does not come close to meeting the professional standard of practice in the field. Professor Rosenthal's approach and the conclusions she draws from it would not be accepted by a peer-reviewed economics journal, and I am, frankly, surprised both that she would submit it to the Court, and that Professors Cutler and McGuire would accept its results as inputs to their analyses.

4. Review of Professor Rosenthal's "Indirect" Model

53. Professor Rosenthal's "indirect" approach is equally flawed, and does not provide a reliable basis for her opinions about a causal relationship between marketing and sales of opioids. Unlike her direct approach, her indirect approach does not include any measure of Defendants' marketing in the model. Instead, she estimates the impact of a number of county-

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level) or individual physicians. *See, e.g.*, Anusua Datta and Dhaval M. Dave, "Effects of Physician-Directed Pharmaceutical Promotion on Prescription Behaviors: Longitudinal Evidence," *Health Economics* 26, 2017, pp. 450–68; Natalie Mizik and Robert Jacobson, "Are Physicians 'Easy Marks'? Quantifying the Effects of Detailing and Sampling on New Prescriptions," *Management Science* 50, no. 12, 2004, pp. 1704–15. These types of "panel data" models allow much more flexibility in controlling for problems such as omitted variables, or constructing instrumental variables to address simultaneity bias. In section IV.A.5, I show how these methods sharply reduce the estimated impact of marketing on sales in a model using county-level data. However, even that model does not fully address simultaneity bias.

[84] Rosenthal Deposition, 355:11–23.

[85] Rosenthal Report, ¶ 103.

[86] Rosenthal Report, ¶ 74.

level demographic, economic, and healthcare characteristics on county-level opioid shipments[87] in 1997. She then uses these 1997 estimates to predict opioid shipments in every year during 1995–2016 and attributes the annual difference between the predicted and actual shipments[88] to Defendants' marketing.

54. Professor Rosenthal's indirect approach is not suited for the purpose she is using it—to establish the "causal" impact of Defendants' marketing. Professor Rosenthal attempts to justify this approach by claiming that it is an "established methodology that has been widely used" in several strands of economics.[89] None of the literature cited by Professor Rosenthal, however, deals with pharmaceutical marketing. Instead, some of the studies cover subjects as far afield as growth accounting for the U.S. economy or factors affecting wage disparities between men and women.[90] A closer review of the literature she cites also reveals that some of the studies do not use an indirect model at all,[91] while others warn that an indirect model does not provide a causal interpretation and instead can produce biased estimates.[92]

55. Professor Rosenthal claims that the volume of prescription opioid shipments that cannot be explained by the factors included in her indirect model must be the result of Defendants'

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[87] Unlike her direct model where the outcome is national-level prescription opioid sales derived from IQVIA data on dispensed opioid prescriptions, Professor Rosenthal's indirect model uses county-level shipments of prescription opioids derived from publicly available ARCOS data. While the IQVIA data identify individual drug products and allow Professor Rosenthal to limit her analysis to certain prescription opioid products, the ARCOS data is at the drug molecule level and does not allow for identification and exclusion of individual drug products. As Professor Rosenthal acknowledges, this results in differences between the ARCOS data she uses in her indirect model and the IQVIA data she uses in her direct model. Specifically, her ARCOS data may include MMEs associated with Schedule III products even though her goal was to exclude such products. *See* Rosenthal Report, ¶ 83.

[88] Because available ARCOS data on prescription opioid shipments only start in 1997, Professor Rosenthal calculates "actual" shipments for 1995–1996 using IQVIA data on prescription opioid sales and scaling those data based on the average annual difference between IQVIA sales and ARCOS shipments in subsequent years.

[89] Rosenthal Report, ¶ 82.

[90] Robert M. Solow, "Technical Change and the Aggregate Production Function," *The Review of Economics and Statistics* 39, no. 3, 1957, pp. 312–20; Nicole Fortin, Thomas Lemieux, and Sergio Firpo, "Decomposition Methods in Economics," in D. Card and O. Ashenfelter, eds., *Handbook of Labor Economics*, 4th Edition, North Holland: Elsevier, pp. 1–102.

[91] Robert M. Solow, "Technical Change and the Aggregate Production Function," *The Review of Economics and Statistics* 39, no. 3, 1957, pp. 312–20; Nicole Fortin, Thomas Lemieux, and Sergio Firpo, "Decomposition Methods in Economics," in D. Card and O. Ashenfelter, eds., *Handbook of Labor Economics*, 4th Edition, North Holland: Elsevier, pp. 1–102.

[92] David M. Cutler, Dahlia Remler, and Joseph P. Newhouse, "Are Medical Prices Declining? Evidence from Heart Attack Treatments," *Quarterly Journal of Economics* 113, no. 4, 1998, pp. 991–1024 at pp. 1013–14; Joseph P. Newhouse, "Medical Care Costs: How Much Welfare Loss?," *Journal of Economic Perspectives* 6, no. 3, 1992, pp. 3–21; A. Craig MacKinlay, "Event Studies in Economics and Finance," *Journal of Economic Literature* 35, 1997, pp. 13–39 at pp. 32–36.

marketing (all of which she assumes is unlawful). The obvious problem with this approach is that factors other than Defendants' marketing that are also omitted from consideration could account for some (or all) of the unexplained component of shipments. The economics literature, including some of the studies cited by Professor Rosenthal, have pointed out that what remains unexplained by such indirect models can be a multitude of different unmeasured factors.[93] Indeed, because this unexplained component is just that—unexplained—it has been called a "measure of our ignorance."[94]

56. Professor Rosenthal also makes no effort to rule out other factors omitted from her indirect model apart from Defendants' marketing. Professor Rosenthal asserts that the demographic, economic, and healthcare characteristics she includes in her model "parallel those used in research literature in this field."[95] Yet she fails to acknowledge that the literature she cites in support of this statement includes a number of other healthcare characteristics that are not included in her model, *e.g.*, prevalence of chronic joint pain and sciatic pain, mental distress, body mass index, number of hospital beds, and number of non-federal physicians, among others.[96]

57. Professor Rosenthal's indirect model also does not attempt to incorporate any of the important drivers of opioid prescriptions discussed in Section IV.A.2 above. These drivers of prescribing behavior are also likely to have driven, at least in part, the increase in opioid shipments during the relevant period. By failing to include these factors in her indirect model, Professor Rosenthal inflates the portion of opioid shipments that remains "unexplained" by the factors she does include. Professor Rosenthal claims incorrectly that all of these "unexplained"

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[93] David M. Cutler and Ellen Meara, "The Technology of Birth: Is It Worth It?" in *Frontiers in Health Policy Research*, Volume 3, ed. Alan M. Garber (Cambridge, MA: The MIT Press, 2000), pp. 39–42; Joseph P. Newhouse, "Medical Care Costs: How Much Welfare Loss?," *Journal of Economic Perspectives* 6, no. 3, 1992, pp. 3–21 at p. 11; Robert E. Hall, Olivier Jean Blanchard, and R. Glenn Hubbard, "Market Structure and Macroeconomic Fluctuations," *Brookings Papers on Economic Activity* 1986, no. 2, pp. 285–338.

[94] Moses Abramovitz, "The Search for the Sources of Growth: Areas of Ignorance, Old and New," *The Journal of Economic History* 53, no. 2, 1993, pp. 217–43 at p. 219.

[95] Rosenthal Report, ¶ 84.

[96] Anne Case and Angus Deaton, "Rising Morbidity and Mortality in Midlife among White Non-Hispanic Americans in the 21st Century," *Proceedings of the National Academy of Sciences* 112, no. 49, 2015, pp. 15078–83 ("Case and Deaton (2015)"); Anne Case and Angus Deaton, "Mortality and Morbidity in the 21st Century," *Brookings Papers on Economic Activity*, 2017, pp. 397–476 ("Case and Deaton (2017)"); Christopher Ruhm, "Deaths of despair or drug problems?" National Bureau of Economic Research Working Paper No. w24188, 2018.

shipments are due to Defendants' marketing (which, again, she wrongly equates with unlawful marketing) without ruling out the possibility that they are likely explained in whole or in part by the drivers of physician prescribing behavior that Professor Rosenthal ignores. Thus, consistent with the view of the economics literature on indirect models, Professor Rosenthal's attempt to use such a model to infer the impact of Defendants' (allegedly unlawful) marketing amounts to no more than a measure of her ignorance of how the larger set of factors omitted from her model impacts shipments. Put another way, the effect, if any, of Defendants' marketing is irrevocably conflated with other factors influencing opioid use that are either not included in her model, or at best, are poorly measured.[97]

58. Finally, although her model can generate county-specific results, Professor Rosenthal inexplicably generates an estimate for the "average" county included in her analysis.[98] Given that Professor Rosenthal provides her estimates to Professor Cutler for purposes of estimating the impact of Defendants' alleged misconduct on *just the Plaintiff Counties*, she should have used her model to generate estimates for those two counties based on their specific economic, demographic, and healthcare characteristics. Had Professor Rosenthal done so, she would have estimated fewer "excess" opioid MMEs for the Plaintiff Counties. Specifically, during the period 2006–2016, the county-specific estimate of "excess" opioid MMEs for Summit County is between [redacted] percentage points lower than the estimate Professor Rosenthal provided to Professor Cutler based on the average impact across all 404 counties included in her indirect model. For Cuyahoga County, the county-specific estimate of "excess" opioid MMEs is between [redacted] percentage points lower than the estimate Professor Rosenthal provides to Professor Cutler.

5. County-Level Direct Model for Ohio

59. As described above, academic researchers typically do not estimate the relationship between pharmaceutical marketing and sales using highly aggregate data like Professor

[97] Another methodological problem with Professor Rosenthal's indirect model is that it is built on the assumption that the impact of the economic, demographic, and healthcare characteristics that Professor Rosenthal does include in her model does not vary over time. Professor Rosenthal provides no justification for this assumption.

[98] To generate this estimate, Professor Rosenthal takes a population-weighted average of each demographic, economic, and healthcare characteristic across the counties, thus ignoring that her own model identified differences in these characteristics as important drivers of the differences in prescription opioid shipments across counties.

Rosenthal does; instead they analyze the variation in marketing and sales at a much more disaggregate level. For example, a county-level analysis allows one to account for other county-specific factors that could simultaneously affect both opioid sales and detailing visits. These include the demographic and socioeconomic characteristics that Professor Rosenthal includes in her indirect model. These also include other unobservable, time-invariant county characteristics that the economics literature typically accounts for through so-called cross-sectional "fixed" effects.[99]

60. A county-level analysis also allows one to account for nationwide trends over time that could simultaneously impact opioid sales and sales representatives' visits across all counties—for example, any general change in norms around pain treatment over time or information about opioid products' risks and benefits from clinical literature.[100] The economics literature typically accounts for these types of time-varying factors through so-called time "fixed effects" or linear and quadratic time trends.[101] In fact, Professor Rosenthal has done this herself in her academic research[102]—in contrast to the methodology she adopted in her expert report. Omitting such factors, as Professor Rosenthal does in her model, would also cause the estimated impact of sales representatives' visits to be biased.

61. I estimate such a model on the 88 counties in Ohio, using the same annual, county-level ARCOS data on shipments of prescription opioids that Professor Rosenthal used for her indirect model. I also measure total opioid shipments the same way Professor Rosenthal did, and include

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[99] *See, e.g.*, Colette DeJong et al., "Pharmaceutical Industry-Sponsored Meals and Physician Prescribing Patterns for Medicare Beneficiaries," *JAMA Internal Medicine* 176, no. 8, 2016, pp. 1114–22; Anusua Datta and Dhaval M. Dave, "Effects of Physician-Directed Pharmaceutical Promotion on Prescription Behaviors: Longitudinal Evidence," *Health Economics* 26, 2017, pp. 450–68 at p. 457; Bradley T. Shapiro, "Informational Shocks, Off-Label Prescribing and the Effects of Physician Detailing," *Management Science* 64, no. 12, pp. 5925–45.

[100] As discussed in Section IV.A.2, various factors could affect opioid prescribing norms while at the same time affecting Defendants' marketing decisions. Examples include the adoption of pain as a fifth vital sign, trends in insurance coverage and reimbursement of different types of pain treatment, increased reliance on patient satisfaction surveys to measure provider quality and determine reimbursement, and the widespread reporting of opioid abuse, addiction, and overdoses that has occurred since 2001.

[101] *See, e.g.*, Pierre Azoulay, "Do Pharmaceutical Sales Respond to Scientific Evidence?," *Journal of Economics & Management Strategy* 11, no. 4, pp. 551–94; Anusua Datta and Dhaval M. Dave, "Effects of Physician-Directed Pharmaceutical Promotion on Prescription Behaviors: Longitudinal Evidence," *Health Economics* 26, 2017, pp. 450–68; Ian Larkin et al., "Restrictions on Pharmaceutical Detailing Reduced Off-Label Prescribing of Antidepressants and Antipsychotics in Children," *Health Affairs* 33, no. 6, 2014, pp. 1014–23; John A. Rizzo, "Advertising and Competition in the Ethical Pharmaceutical Industry: The Case of Antihypertensive Drugs," *Journal of Law and Economics* 42, 1999, pp. 89–116.

[102] Rosenthal et al. (2003).

in the model the same demographic, economic, and healthcare characteristics that Professor Rosenthal included in her indirect model.[103]

62. To measure marketing, I rely on Purdue's internal database of sales representatives' "call notes" from visits to Ohio physicians. This tracks the number of detailing visits per year in each county.[104] This measure excludes marketing by other Defendants and non-Defendants, and therefore likely overestimates the impact of Purdue's detailing visits. Specifically, to the extent Purdue sales representatives are more likely to make detailing visits in counties where other opioid manufacturers' sales representatives are also likely to make such visits, the model will attribute the effects of other opioid manufacturers' detailing visits on total opioid shipments to Purdue's detailing visits.

63. To estimate the potential impact of past marketing on current year's sales, I allow for a separate impact of detailing visits from each year in the past. This is a more flexible approach than the one employed by Professor Rosenthal because it does not require marketing to depreciate at a constant rate. This approach also allows me to test how long the impact of past marketing actually lasts. For the reasons described above, I also include county and year fixed effects.

64. The results from this model are displayed in Exhibit 1. As Exhibit 1 illustrates, the impact of Purdue's marketing is nowhere near as long-lasting as Professor Rosenthal's flawed direct model predicts. Specifically, the data show that Purdue sales representatives' visits to physicians only impact opioid sales in the same year and have no impact in future years. As discussed above, this relatively high "depreciation rate" of promotion is in line with the findings of the economics literature. The size of the impact is also in line with the findings in the economics literature, including those of Professor Rosenthal's academic research.[105]

65. It is important to note that while this model addresses a number of flaws in Professor Rosenthal's direct methodology, it still does not provide an estimate of the "causal" impact of Purdue's marketing on opioid sales—let alone the impact of "unlawful" marketing. As discussed

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[103] Rosenthal Report, ¶¶ 83–85.

[104] I limited my analysis to only opioid-related detailing visits based on information provided in the "ProductsPresented" and "Products" data fields.

[105] My results are qualitatively and quantitatively similar if I instead estimate the model by measuring sales representatives' visits and opioid sales on a quarterly basis. This is the most disaggregate level at which the ARCOS data on prescription opioid shipments are available.

above, lack of county-level data on detailing by any other opioid manufacturer is likely to cause an upward bias in the estimated impact of Purdue's detailing. Similarly, the model does not address the issue of simultaneity (Purdue's detailing not only impacting but also reacting to current and anticipated Purdue sales). This, as discussed above, is also likely to cause an upward bias in the estimated impact, and is widely recognized as a major problem in the literature estimating the impact of pharmaceutical marketing—though ignored by Professor Rosenthal. Lastly, for comparison purposes, this model measures aggregate opioid sales (in terms of total opioid MMEs shipped to each Ohio county) and hence, like Professor Rosenthal's model, conceals economically important variation across opioid products.

66. Setting those issues aside, one could still compare the "excess" MMEs predicted by this model for the two Plaintiff Counties with the "excess" MMEs predicted by Professor Rosenthal's model. [redacted]

B. Professor Rosenthal's Review of Academic Literature and Other Empirical Research Studying the Impact of Prescription Drug Marketing

67. As conceptual foundation to her report and the analysis discussed above, Professor Rosenthal describes the findings from the clinical and economics literature examining the impact of pharmaceutical promotion, as well as Defendants' internal assessments of marketing impacts. Her review of these materials is highly selective, however, and she frequently mischaracterizes the findings from these studies. As touched upon above and discussed more fully below, these errors further undermine her opinions.

1. Evidence from the Clinical Literature

68. Based on the clinical literature, Professor Rosenthal opines that physicians are time-constrained and susceptible to easily accessible information, even when that information is not accurate.[106] She implies that, as a result, physicians may be unduly influenced by the marketing tactics of opioid manufacturers. As Professor Rosenthal points out, there have indeed been "numerous studies in the clinical literature on the impact of promotion on physician beliefs, knowledge and self-reported behavior."[107] However, the particular way in which she chooses to "highlight a few of the most salient examples of this extensive literature"[108] results in a very one-sided view of a complex phenomenon. Moreover, Professor Rosenthal draws conclusions from these studies that omit important qualifications made by the original authors, or are at odds with those drawn by the authors in the cited paper or in follow-up research. Many of the studies cited by Professor Rosenthal are directly contradicted by other empirical research or suffer from severe methodological flaws.

69. For example, Professor Rosenthal cites a 1982 paper by Avorn, Chen, and Hartley.[109] In it, the authors conclude that physicians do not adequately recognize their vulnerability to commercial influences.[110] She fails, however, to cite a number of other papers with contradictory findings:

a. Beltramini and Sirsi (1992), who conclude that physicians found information from professional colleagues much more "believable" than information from sales people or advertisements;[111]

b. Peay and Peay (1990), who report that out of fifteen potential information

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[106] Rosenthal Report, ¶ 14.
[107] Rosenthal Report, ¶ 28.
[108] Rosenthal Report, ¶ 28.
[109] Jerry Avorn et al., "Scientific versus Commercial Sources of Influence on the Prescribing Behavior of Physicians," *The American Journal of Medicine* 73, no. 1, 1982, pp. 4–8.
[110] Jerry Avorn et al., "Scientific versus Commercial Sources of Influence on the Prescribing Behavior of Physicians," *The American Journal of Medicine* 73, no. 1, 1982, pp. 4–8.
[111] Richard F. Beltramini and Ajay K. Sirsi, "Physician Information Acquisition and Believability: A Field Experiment on Source and Type of Information," *Journal of Health Care Marketing* 12, no. 4, 1992, pp. 52–59 at p. 56.

sources about drugs, physicians rated information provided by sales representatives only twelfth in usefulness;[112]

c. Lichtstein et al. (1992) and McKinney et al. (1990), who find that physicians have skeptical or negative views about pharmaceutical promotion;[113]

d. Connelly et al. (1990), who find that physicians view information from pharmaceutical sales representatives as having the least credibility relative to information from a range of other sources such as textbooks, original research published in journals, clinical manuals, and colleagues in their own or other subspecialties.[114]

e. Anderson et al. (2009), who find that physicians favor journal articles, colleagues, and continuing medical education over pharmaceutical sales representatives as sources of prescribing information.[115]

70. Professor Rosenthal also states that clinical research has demonstrated a positive impact of promotional effort and company-sponsored educational events on formulary requests, prescribing of newer drugs over older drugs, and prescribing of specific products that are being promoted. Yet, she offers only two studies to support these claims, both of which suffer from severe methodological limitations.[116] Chren and Landefeld (1994) examined the association between physician interactions with pharmaceutical companies and requests for formulary adjustments at a single teaching hospital, and acknowledged that their study was not designed to

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[112] Marilyn Y. Peay and Edmund R. Peay, "Patterns of Preference for Information Sources in the Adoption of New Drugs by Specialists," *Social Science and Medicine* 31, no. 4, 1990, pp. 467–76 at p. 470–71.
[113] Peter R. Lichstein et al., "Impact of Pharmaceutical Company Representatives on Internal Medicine Residency Programs: A Survey of Residency Program Directors," *Archives of Internal Medicine* 152, no. 5, 1992, pp. 1009–13; W. Paul McKinney, "Attitudes of Internal Medicine Faculty and Residents toward Professional Interactions with Pharmaceutical Sales Representatives," *Journal of the American Medical Association* 264, no. 13, 1990, pp. 1693–97.
[114] Donald P. Connelly et al., "Knowledge of Resource Preferences of Family Physicians," *Journal of Family Practice* 30, no. 3, 1990, pp. 353–59.
[115] Britta L. Anderson et al., "Factors Associated With Physicians' Reliance on Pharmaceutical Sales Representatives," *Academic Medicine* 84, no. 8, 2009, pp. 994–1002 at p. 997.
[116] Rosenthal Report, ¶ 31, FN 48–50, citing Peay and Peay (1988) and Chren and Landefeld (1994).

identify a causal relationship.[117] The study by Peay and Peay (1988) was likewise very limited in scope. It was based on interviews that asked physicians to qualitatively assess whether they had heard of the drug, the sources from which they heard about it, and whether they prescribed the product.[118] This analysis was limited to a very small sample of 124 physicians, over three decades ago, for a single product, and among Australian, not U.S. doctors, living in the vicinity of a single Australian city.[119] In addition to these two individual studies, Professor Rosenthal also cites a review article which provided an overview of a number of clinical studies.[120] Not only does this review demonstrate that many clinical studies found no association between pharmaceutical promotion and increased prescribing, but the authors specifically note that all the reviewed studies had design limitations such that the studies "measure associations but [do] not prove causation" and that "causality may be bidirectional."[121]

71. In sum, Professor Rosenthal presents only a highly selective and one-sided review of the clinical literature to support the opinion she wants to reach—that doctors' decisions are controlled by pharmaceutical marketing. At the same time, she ignores contradictory data which confirm that doctors are, as one would expect, highly trained and skilled professionals who rely on a range of information, including their experience and knowledge gained from medical training, as well as other scientific resources to make responsible prescribing choices for their patients.

2. Evidence from the Economics Literature

72. Professor Rosenthal also cites a number of academic studies from the economics literature that have found a positive association between measures of aggregate marketing (*i.e.*, not limited to allegedly unlawful marketing) and measures of drug sales. Professor Rosenthal

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[117] Mary Margaret Chren and Seth Landefeld, "Physicians' Behavior and Their Interactions with Drug Companies: A Controlled Study of Physicians Who Requested Additions to a Hospital Drug Formulary," *The Journal of the American Medical Association* 271, no. 9, 1994, pp. 684–89 at pp. 684, 689.
[118] Marilyn Y. Peay and Edmund R. Peay, "The Role of Commercial Sources in the Adoption of a New Drug," *Social Science & Medicine* 26, no. 12, 1988, pp. 1183–89 at p. 1185.
[119] Marilyn Y. Peay and Edmund R. Peay, "The Role of Commercial Sources in the Adoption of a New Drug," *Social Science & Medicine* 26, no. 12, 1988, pp. 1183–89 at pp. 1183–85.
[120] Geoffrey K. Spurling et al., "Information from Pharmaceutical Companies and the Quality, Quantity, and Cost of Physicians' Prescribing: A Systematic Review," *PLoS Medicine* 7, no. 10, 2010, pp. 4, 12–17.
[121] Geoffrey K. Spurling et al., "Information from Pharmaceutical Companies and the Quality, Quantity, and Cost of Physicians' Prescribing: A Systematic Review," *PLoS Medicine* 7, no. 10, 2010, pp. 11, 17.

fails to acknowledge, however, that researchers have not, in general, found compelling evidence of a strong, direct, causal link between promotional efforts and substantial changes in physician prescribing behavior. To the contrary, the literature suggests that the identifiable causal effect of promotion on prescribing is often either statistically insignificant or quite small. The peer-reviewed studies published in reputable journals that have found evidence of a statistical association between promotion and prescribing typically do not make a claim that this is evidence of a causal relationship—if the authors tried to do so, it would be red-flagged in peer review and would have to be removed before the study could be accepted for publication.

73. The economics literature, including some of the papers Professor Rosenthal cites, note that proving causation in the context of advertising is especially difficult. DellaVigna and Gentzkow (2010) point out that while there is a large literature studying correlations between monthly or annual measures of aggregate advertising intensity and sales, interpreting the results from this literature is difficult.[122] The authors specifically warn that these results do not have a clear causal interpretation as reverse causality may be at play, or sales and promotion may both be determined by other factors.

74. As with her selective review of the clinical literature, Professor Rosenthal offers a similarly selective review of the economics literature that estimates the size of the impact of pharmaceutical marketing. In particular, Professor Rosenthal's review of the literature fails to acknowledge the large body of research that presents a much more muted assessment of the size of the impact of pharmaceutical marketing. A number of studies, including some co-authored by Professor Rosenthal, show that the effect of promotion on prescribing is limited or non-existent. For instance, Professor Rosenthal's 2004 study on the role of promotion on sales of antidepressants found that "[n]either the detailing spending for the drug taken nor the detailing spending for the other drugs in the class had any significant effect on the duration of treatment with an antidepressant medication."[123] This study also found no effect of promotion to physicians on treatment initiation with an antidepressant medication.[124] In another study on the role of

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[122] Stefano DellaVigna and Matthew Gentzkow, "Persuasion: Empirical Evidence," *Annual Review of Economics* 2, no. 1, pp. 643–69.

[123] Julie M. Donohue et al., "Effects of Pharmaceutical Promotion on Adherence to the Treatment Guidelines for Depression," *Medical Care* 42, no. 12, 2004, pp. 1176–85 at p. 1179.

[124] Julie M. Donohue et al., "Effects of Pharmaceutical Promotion on Adherence to the Treatment Guidelines for

promotion on five therapeutic drug classes Professor Rosenthal found no statistically significant impact of either product-level direct-to-consumer advertising or physician detailing on product-level sales.[125] In the same study, Professor Rosenthal did find a statistically significant impact of class-wide detailing on class-wide sales but the size of the estimates were modest—a one percent increase in detailing was associated with a 0.017 to 0.034 percent increase in sales.[126]

75. Professor Rosenthal's review of the economics literature also ignores a large body of academic research that supports the notion of strong depreciation of pharmaceutical advertising, *i.e.*, that the effects of marketing wear off quite quickly over time (contrary to Professor Rosenthal's opinions discussed above). For example, a 2002 study by King on the promotion of ulcer medications estimated an annual depreciation rate for marketing of 60 percent.[127] The 2018 study by Shapiro mentioned above found that the effect of detailing on the prescribing behavior of nearly two thousand primary care physicians and psychiatrists "appears to taper off completely by three months after the visit."[128] Other studies concerning detailing's long-term effects on the prescribing of drugs have found similarly high rates of depreciation.[129]

76. In sum, Professor Rosenthal presents a distorted review of the literature on the size of the impact of pharmaceutical marketing. Contrary to Professor Rosenthal's depiction, the literature in fact concludes that the impact is small, variable, and dissipates over time.

3. Evidence from Literature Specific to Prescription Opioids

77. Professor Rosenthal claims that "[t]he opioid epidemic has spurred both investigative journalism and academic research into the causes of increased opioid prescribing,"[130] and that

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Depression," *Medical Care* 42, no. 12, 2004, pp. 1176–85 at pp. 1176, 1179.

[125] Rosenthal et al. (2003), p. 17.

[126] Rosenthal et al. (2003), p. 21.

[127] Charles King III, "Marketing, Product Differentiation, and Competition in the Market for Antiulcer Drugs," *HBS Working Paper* No. 01-014, September 16, 2002, p. 17.

[128] Bradley T. Shapiro, "Informational Shocks, Off-Label Prescribing and the Effects of Physician Detailing," *Management Science* 64, no. 12, pp. 5925–45.

[129] Oliver Richard and Larry Van Horn, "Persistence in Prescriptions of Branded Drugs," *International Journal of Industrial Organization* 22, 2004, pp. 523–40 at p. 525; Natalie Mizik and Robert Jacobson, "Are Physicians 'Easy Marks'? Quantifying the Effects of Detailing and Sampling on New Prescriptions," *Management Science* 50, no. 12, 2004, pp. 1704–15, pp. 1710; Marc Fischer and Sönke Albers, "Patient- or Physician-Oriented Marketing: What Drives Primary Demand for Prescription Drugs," *Journal of Marketing Research* 47, 2010, pp. 103–21.

[130] Rosenthal Report, ¶ 39.

this opioid-specific literature is further support for her opinions. However, none of the sources she cites in support of this statement establishes a causal relationship between promotional efforts of opioid drug manufacturers and opioid sales. Of the four studies that Professor Rosenthal cites, only two include a statistical model, and each of these two studies makes clear that the study's results cannot be used to make causal claims.

78. In particular, Hadland et al. (2018) explicitly note that their findings only demonstrate "an association, not cause and effect," and that their study cannot exclude the possibility of reverse causation.[131] The New York State Health Foundation similarly explains that its study "cannot conclusively determine a causal link" between industry payments and increases in opioid prescribing as "[i]t is possible that changes in drug prescribing reflect changes in physicians' patient panels (e.g., they are treating more patients who require pain management) or in specific patients' needs, rather than other influences such as opioid-related payments."[132]

79. The other two studies Professor Rosenthal cites do not measure a relationship at all, let alone measure a causal relationship. For example, Professor Rosenthal claims that "[Van] Zee identifies a number of other promotional activities that contributed to the increase in [opioid] sales," but she fails to acknowledge that Van Zee (2009) did not include **any** analysis on the impact of said promotional activities on sales. Instead, the author simply reported statistics on the size of OxyContin sales, as well as statistics on the types and size of certain Purdue promotional activities.[133] The last study mentioned by Professor Rosenthal, also by Hadland et al. (2017), documented payments to physicians in connection with opioid products. But, again,

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[131] Scott E. Hadland et al., "Association of Pharmaceutical Industry Marketing of Opioid Products to Physicians with Subsequent Opioid Prescribing," *JAMA Internal Medicine* 178, no. 6, 2018, pp. 861–63. Dr. Hadland and other co-authors have a 2019 article that also estimates the relationship between opioid marketing and prescribing. The results presented in Table 3 of that article purport to be adjusted relative risks but that cannot be the case as many of the estimates are negative. As a result, it is not possible to evaluate the size of the estimated relationship from that article. Moreover, similar to Hadland et al. (2018), the authors note that they demonstrate "associations between opioid marketing and subsequent prescribing" and they "cannot exclude reverse causation." *See* Scott E. Hadland et al., "Association of Pharmaceutical Industry Marketing of Opioid Products With Mortality From Opioid-Related Overdoses," *JAMA Network Open* 2, no. 1, 2019, pp. 1–12.

[132] "Follow the Money: Pharmaceutical Manufacturer Payments and Prescribing Patterns in New York State," New York State Health Foundation Report, June 2018.

[133] Art Van Zee, "The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy," *American Journal of Public Health* 99, no. 2, 2009, pp. 221–27. I note that Dr. Van Zee is a primary care physician, and has no formal training or qualifications in epidemiology, economics, or marketing.

the authors did not conduct any analyses to examine the effects of these payments on physicians' prescribing behavior.[134]

4. Evidence from Purdue's Internal Studies on the Effectiveness of Its Promotion

80. Professor Rosenthal presents a similarly selective review of Purdue's internal studies when she claims that Defendants' return on investment ("ROI") is consistently high.[135] Purdue's internal studies, in fact, confirm the literature's findings of a variable and small impact of pharmaceutical marketing on prescriptions.

81. To begin with, Purdue's internal studies identified substantial variation in promotional effectiveness across different programs. For example, Purdue noted in some of its analyses that there are a number of "not performing" programs such as "Trigger Mail," "Member Health" and "Journal Ads." Further, while other programs such as "Savings Cards" were found to be effective in some analyses, Purdue noted that they all have diminishing returns.[136]

82. Purdue's internal studies also show that promotional effectiveness differs across prescribing populations. For example, primary specialists, as opposed to primary care physicians, nurse practitioners, and physician assistants, are found to be "much more responsive" to detailing,[137] which supports the academic literature's findings that differently situated doctors process and use information differently. Moreover, Purdue noted that even if detailing of some prescribers "generate[s] [prescriptions] lift," the detailing does not necessarily "breakeven" in terms of ROI, and additional detailing visits to the same physicians were less effective than initial visits.[138] Indeed, as discussed above, Purdue's assessment of the number of OxyContin prescriptions generated by one detailing visit was as low as 0.1 prescriptions and at most 5

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[134] Scott E. Hadland et al., "Industry Payments to Physicians for Opioid Products, 2013–2015," *American Journal of Public Health* 107, no. 9, 2017, pp. 1493–95.
[135] Rosenthal Report, ¶ 45.
[136] Purdue Presentation, "OxyContin: Marketing Mix Modeling Result," July 2012, PPLP003409899–935 at 904; Psyma International, Inc. Report, "OxyContin® Patient Copay Study: Final Report," May 21, 2007, PPL003417916–59 at 52.
[137] Purdue Presentation, "OxyContin: Marketing Mix Modeling Result," July 2012, PPLP003409899–935 at 912.
[138] Purdue Presentation, "OxyContin: Marketing Mix Modeling Result," July 2012, PPLP003409899–935 at 904.

prescriptions, where the effectiveness depended on the physician's specialty and the level of their already-existing prescribing activity.[139]

83. In addition to measuring the effectiveness of various detailing programs, Purdue has also conducted event impact studies to measure the effects of specific marketing events on the prescribing rates of attending healthcare providers. Examples of events studied include conferences, targeted marketing campaigns, and dinner events. These studies track changes in the prescribing rates of attendees before and after the event, and compare these to changes in the prescribing rates of non-attendees over the same period. An ROI is then calculated based on the incremental prescriptions that Purdue linked to the event and the event's cost. Results from these event impact studies exhibit substantial variation as well, including instances of negative ROIs.[140]

84. In sum, the available research on the effects of pharmaceutical promotion do not lend support to Professor Rosenthal's model results that Defendants' marketing had large, consistent, and sustained effects on prescription opioid sales. Professor Rosenthal's flawed modeling is mirrored in her flawed review of the literature, and is called into question by Purdue's own findings that the effectiveness of marketing is small, variable, and dissipates over time.

C. Review of Professor Rosenthal's Analysis of "Under-Treated" Pain

85. Professor Rosenthal's assessment of the impact of "under-treated" pain is also flawed and unscientific because her analysis consists of making a strong and unsupported assumption that predetermines her ultimate finding. Specifically, Professor Rosenthal purports to investigate to what extent "under-treated" pain can explain the nationwide trend in opioid prescribing since 1995.[141] To do so, she starts by defining the patient populations with potentially under-treated pain as only two types of patients—cancer patients at the end of life or receiving hospice care,

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[139] Purdue Presentation, "Marketing Mix Modeling Result," July 2012, PPLP003409899_PPLP002 at 912–17; Purdue Presentation, "OxyContin Marketing Mix," PPLP003409951_PPLP002 at 68–73.
[140] See, *e.g.*, Purdue Presentation, "OxyContin Abuse Deterrent Messaging Program -- Topline," March 7, 2014, PPLP003409939–50; Purdue Presentation, "Dinner and Teleconference Program Impact: Preliminary Analysis," November 2010, PPLP003409715–22; Forecasting, Analytics & Market Research Presentation, "OxyContin Pri-Med (West) Conference Impact," January 17, 2012, PPLP003410223–35.
[141] Rosenthal Report, ¶ 81.

and patients with acute pain due to either trauma or surgery.[142] Professor Rosenthal then proceeds to calculate the "theoretical maximum, scientifically-accepted use of opioids" among these patients by estimating the national, annual prevalence of these two groups and applying certain assumptions about the average dosing and duration of opioid treatment for each group.[143] This allows Professor Rosenthal to arrive at an estimate for the level of "clinically justifiable" opioid sales in the U.S. from 1995 through 2018 that is less than [redacted] percent of the actual level of opioid sales (both measured in MMEs) observed during this period.[144]

86. This finding depends crucially on Professor Rosenthal's definition of "clinically justifiable" uses of opioids, and in particular her assumption that cancer patients at the end of life and patients suffering from acute pain due to trauma and surgery are the **only** patients for whom there is any "clinically justifiable" use of opioids. This assumption is divorced from (and indeed runs contrary to) the FDA-approved uses of prescription opioids as reflected in these drugs' labels. As discussed earlier, the FDA, the agency tasked with evaluating the benefits and risks of all prescription drugs, including opioids, has never limited the use of prescription opioids to just the two uses that Professor Rosenthal chooses to include in her definition of "clinically justifiable" uses.[145] On the contrary, as discussed earlier, the FDA has resisted calls to restrict the use of opioids in the manner that Professor Rosenthal attempts to do in her report.

87. Professor Rosenthal's definition of clinically justifiable uses also contradicts the CDC 2016 Guideline on chronic pain. Professor Rosenthal is aware of the CDC 2016 Guideline as evidenced by her reliance on this document when determining the appropriate duration of opioid treatment for *acute pain*.[146] Yet, she ignores that the primary purpose of this guideline is to provide "recommendations for primary care clinicians who are prescribing opioids for *chronic pain* outside of active cancer treatment, palliative care, and end-of-life care."[147] As defined by the CDC, chronic pain is pain that typically lasts more than three months and requires outpatient treatment.[148] Specifically, while the CDC 2016 Guideline notes that "opioids should not be

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[142] Rosenthal Report, ¶¶ 95–99.
[143] Rosenthal Report, ¶ 94 and Attachment D.
[144] Rosenthal Report, Table 6.
[145] FDA letter to Andrew Kolodny, September 10, 2013.
[146] Rosenthal Report, FN 128, 132.
[147] CDC 2016 Guideline, pp. 1–49 at p. 1 (emphasis added).
[148] CDC 2016 Guideline, pp. 1–49 at p. 2.

considered first-line or routine therapy for chronic pain," the guideline also notes that neither should chronic pain patients be "required to sequentially 'fail' nonpharmacologic and nonopioid pharmacologic therapy before proceeding to opioid therapy."[149] In other words, the CDC 2016 Guideline envisions the use of opioid therapy for some chronic pain patients and even notes that in certain clinical contexts "opioids might be appropriate [treatment for chronic pain] regardless of previous therapies used."[150]

88. Professor Rosenthal's narrow definition of clinically justifiable uses similarly ignores that prescription opioids continue to be prescribed by physicians and continue to be reimbursed by both private and public payors for chronic pain. For example, a 2018 analysis conducted by the CMS shows that chronic pain was one of the top ranked conditions most often associated with high dose opioid utilization among Medicare beneficiaries and dual Medicare and Medicaid beneficiaries.[151] Further, the claims data produced by Plaintiffs show that as recently as 2018, Plaintiffs or other third party payors acting on their behalf continued to reimburse prescriptions for opioids, including OxyContin, for individuals diagnosed with chronic pain.[152] Indeed, even Plaintiffs' expert, Dr. Alexander, a practicing general internist and Professor of Epidemiology and Medicine, testified that opioids can be appropriate for chronic pain (consistent with OxyContin's FDA-approved label).[153]

89. Given the "substantial" size of the U.S. population suffering from chronic pain,[154] and the relatively small population of cancer patients, it is no wonder that Professor Rosenthal's assumption that non-cancer chronic pain is a clinically unjustifiable use of opioids leads her to find that clinically justifiable uses account for only a small share of opioid shipment MMEs. By

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[149] CDC 2016 Guideline, pp. 1–49 at p. 16.
[150] CDC 2016 Guideline, pp. 1–49 at p. 16.
[151] Karyn Kai Anderson et al., "National Trends in High-Dose Chronic Opioid Utilization among Dually Eligible and Medicare-Only Beneficiaries (2006–2015)," *CMS Data Brief*, October 2018.
[152] Cuyahoga and Summit County Medical and Pharmacy Claims Data; Dora H. Lin et al., "Prescription Drug Coverage for Treatment of Low Back Pain Among US Medicaid, Medicare Advantage, and Commercial Insurers," *JAMA Network Open* 1, no. 2.
[153] Deposition of G. Caleb Alexander, April 26, 2019 ("Alexander Deposition"), 31:24–32:6. In addition, Plaintiffs' FDA expert, Dr. Kessler, noted that "there is a small fraction of chronic pain patients with pain of nonmalignant origin who can also potentially benefit from the product." *See* Deposition of David A. Kessler, April 26, 2019, 547:24–548:3.
[154] CDC 2016 Guideline, pp. 1–49 at p. 1.

making this assumption, Professor Rosenthal predetermines the results of her so-called assessment of under-treated pain and thereby violates a basic tenet of scientific methods.

V. Review of Professor Cutler's Analysis and Opinions

90. Professor Cutler purports to estimate the impact of opioid shipments caused by Defendants' alleged misconduct on harms to the Plaintiffs.[155] This is accomplished in four steps. First, Professor Cutler estimates the share of opioid-related mortality that is, in his opinion, caused by opioid shipments based on an analysis of approximately 400 counties across the U.S.[156] Second, he applies Professor Rosenthal's national estimates of the impact of Defendants' marketing on prescription opioid shipments to estimate the share of opioid-related mortality purportedly caused by Defendants' alleged misconduct.[157] Third, Professor Cutler estimates the share of harms to the Plaintiffs associated with mortality, addiction, crime, and child maltreatment that can be tied to opioids in some way ("opioid-related harms"). Fourth, he assumes that the share of these opioid-related harms caused by Defendants' alleged misconduct is the same as the estimated share of opioid-related mortality that, in his opinion, was caused by Defendants' alleged misconduct.

91. For example, Professor Cutler estimates that in 2006, prescription opioid shipments accounted for [redacted] percent of opioid-related deaths.[158] Based on Professor Rosenthal's analysis, he assumes that manufacturer Defendants' allegedly unlawful conduct caused [redacted] percent of shipments in 2006.[159] Multiplying these two numbers together, Professor Cutler estimates that manufacturer Defendants' alleged misconduct is responsible for [redacted] percent of opioid-related mortality in 2006. He then applies this percent to the share of opioid-related harms he calculates for various divisions of Plaintiff County governments in 2006. For example, he estimates that opioid-related addiction treatment accounted for 3.3 percent of spending by Cuyahoga County's

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[155] Cutler Report, Tables III.16A and III.16B.
[156] Cutler Report, ¶¶ 92, 96. Professor Cutler includes 400 counties in his "direct regression model" sample and 404 counties in his "indirect regression model" sample. I discuss both models in greater detail below.
[157] Cutler Report, Tables III.13 and III.14.
[158] This is calculated by multiplying the coefficient from Professor Cutler's direct regression model (4.39), by cumulative average shipments in 2006 (1.12) and dividing by the actual mortality rate in 2006 (9.97). *See* Cutler Report, Table III.10.
[159] Cutler Report, Table III.9.

Alcohol, Drug Addiction, and Mental Health Services ("ADAMHS") Board.[160] He multiplies this number by [redacted] percent to arrive at his estimate of the share of ADAMHS spending that resulted from manufacturer Defendants' alleged misconduct.[161]

92. I discuss the flaws in Professor Cutler's analyses in the sections that follow. Before doing so, it is important to note what Professor Cutler has not done. To begin with, similar to Professor Rosenthal, he has failed to establish causality (*i.e.*, that the relationship between prescription opioid shipments and opioid-related mortality is causal rather than simply an association). Nor has he analyzed the impact of any particular product on opioid mortality. He also has not attempted to distinguish the impact of immediate-release versus extended-release products, or abuse-deterrent formulations versus non-abuse-deterrent formulations, or different types of opioids (oxycodone versus hydrocodone versus fentanyl, etc.). In addition, Professor Cutler has not attempted to determine what share of shipments resulted in diverted opioids and whether diverted opioids play an outsized role in opioid-related mortality.

93. Data from the National Survey on Drug Use and Health ("NSDUH") show that from 2006 to 2014, 68–76 percent of individuals who used prescription pain relievers non-medically in the past month obtained those pain relievers from a source other than a prescription. Similarly, the data also show that from 2015 to 2017, 60–61 percent of individuals who misused prescription pain relievers most recently obtained those pain relievers from a source other than a prescription. This extensive diversion is consistent with the discrepancy between the ages of those who misuse prescription opioids (younger) and those who properly use them (older). For example, the NSDUH data show that between 2015 and 2017, 53 percent of people misusing prescription pain relievers were under age 35 compared to only 29 percent of people properly using prescription pain relievers. In contrast, people properly using prescription pain relievers were much more skewed towards older ages—48 percent were age 50 or greater, compared to only 23 percent of people misusing prescription pain relievers.[162] These findings reinforce the

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[160] Cutler Report, Table III.5.

[161] Cutler Report, Tables III.5, III.13, and III.16A. Estimates correspond to Professor Cutler's "Approach 1" to estimating the impact of shipments on opioid-related mortality.

[162] In addition to the NSDUH data, the Treatment Episode Data Set: Admission ("TEDS-A"), also maintained by the Substance Abuse and Mental Health Services Administration, contains data on individual admissions to substance abuse treatment facilities that receive federal funding. These data show that among admissions for treatment for abuse of "Other Opiates and Synthetics" between 1996 and 2016, 65 percent involved a patient who first used

conclusion that opioid mortality rates are not being driven by opioid deaths in patients prescribed opioids by their doctors (allegedly influenced by marketing messages overriding their judgment about what is best for each individual patient).

A. Professor Cutler's Direct and Indirect Models

94. Professor Cutler uses two different methods (a "direct" regression model and an "indirect" regression model) to estimate the impact of prescription opioid shipments on opioid-related mortality. The "direct" regression model estimates the relationship between cumulative prescription opioid shipments into a county between 1997 and 2010 and the change in opioid-related mortality in the county between the mid-1990s and 2010. This method is used to estimate both the relationship between shipments and all opioid-related mortality between 2006 and 2010 and the relationship between shipments and licit opioid-related mortality between 2011 and 2016. The "indirect" regression model estimates the relationship between opioid-related mortality and various economic and demographic factors in a "baseline" period and then uses these estimates to predict opioid-related mortality for later periods assuming those same relationships hold. Professor Cutler attributes any difference between actual and predicted opioid-related mortality to prescription opioid shipments. This method is used to estimate the relationship between shipments and illicit opioid-related mortality between 2011 and 2016 and the relationship between shipments and all opioid-related mortality between 2006 and 2016.

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prescription opioids before age 25 and 87 percent before age 35. (TEDS-A data define "Other Opiates and Synthetics" as follows: "buprenorphine, codeine, hydrocodone, hydromorphone, meperidine, morphine, opium, oxycodone, pentazocine, propoxyphene, tramadol, and any other drug with morphine-like effect.") Consistent with this, Cicero et al. (2014) show that the mean age of first opioid use since the 1990s has been around 20–25 (p. 824). In contrast, prescription opioid patients are typically older. For example, Volkow et al. (2011) show that the most common age group of people prescribed opioids is 40–59 years old (46 percent of prescriptions dispensed in 2009 went to people in this age group), followed by 60+ (28 percent of prescriptions dispensed went to people in this age group). Volkow et al. (2011), p. 1299. Similarly, the Kaiser foundation found that the highest opioid prescription rates among those with large employer, private insurance were among patients aged 55–64 (22 percent), followed by 45–54 (19 percent). The rate among the 18–34 age group was only 12 percent. And the CDC studied prescription rates by age group in eight states and found that in each state, the three age groups with the highest opioid prescription rates were 45–54, 55–64, and 65+. *See* Theodore J. Cicero et al., "The Changing Face of Heroin Use in the United States: A Retrospective Analysis of the Past 50 Years," *JAMA Psychiatry* 71, no. 7, 2014, pp. 821–26 at p. 821; Nora D. Volkow et al., "Characteristics of Opioid Prescriptions in 2009," *JAMA* 305, no. 13, 2011, pp. 1299–1301 at p. 1299; Cynthia Cox et al., "A Look at How the Opioid Crisis Has Affected People with Employer Coverage," *Peterson-Kaiser Health System Tracker Brief*, April 5, 2018; Leonard Paulozzi et al., "Controlled Substance Prescribing Patterns—Prescription Behavior Surveillance System, Eight States, 2013," *MMWR Surveillance Summaries* 64, no. 9, 2015, pp. 1–14 at p. 5.

Under his "Approach 1," Professor Cutler combines the results of his direct and indirect regression models to arrive at estimates of the share of opioid-related mortality between 2006 and 2016 that, in his opinion, was caused by prescription opioid shipments. Under his "Approach 2," Professor Cutler relies entirely on the indirect regression model for these estimates. Table 1 summarizes his two approaches and the associated methods he employs.

Table 1: Summary of Professor Cutler's Approaches to Estimating the Relationship Between Shipments and Opioid-Related Mortality

Approach	Time Period	Type of Opioid-Related Mortality	Method Used
Approach 1	2006–2010	All	Direct Regression
	2011–2016	Licit	Direct Regression
	2011–2016	Illicit	Indirect Regression
Approach 2	2006–2016	All	Indirect Regression

1. Direct Regression Model

95. Professor Cutler's direct regression model produces inflated estimates of the impact of prescription opioid shipments on opioid-related mortality because the model fails to account for important factors that affect opioid-related mortality. In particular, he does not account for the social pain, distress, and dysfunction that have led to an increase in drug and alcohol poisonings generally, including opioid-related deaths, both intentional and unintentional, since the late 1990s. These are "deaths of despair" according to Professor Anne Case and Professor and Nobel laureate Angus Deaton, two Princeton University economists who have authored two papers about the topic.[163] Professor Cutler cites these papers in his report.[164] He also peer reviewed the first paper and provided a published comment on the second paper.

96. "Deaths of despair" have arisen, according to Case and Deaton, due to a "cumulative disadvantage" that has plagued the "white working class" since "its heyday in the early

[163] Case and Deaton (2015); Case and Deaton (2017), p. 417. In their 2017 paper, Case and Deaton define deaths of despair as deaths resulting from "drug overdoses, suicide, and alcohol-related liver mortality."
[164] Cutler Report, ¶ 88.

1970s."[165] Some of that disadvantage is due to economic factors such as the decline in real wages for less educated workers.[166] But, as the authors note, "the economic story can account for … only a part [of the increase in 'deaths of despair'], and … it leaves more unexplained than it explains."[167] Rather, larger, "slow-acting social forces" that are difficult to measure directly and can be picked up only to a certain extent in metrics such as income and wages are an important factor to take into account. These forces include "changes in social customs that have allowed dysfunctional changes in patterns of marriage and childrearing," "move[ment] away from the security of legacy religions," "globalization and automation," "the decline of unions," and a general "failure of life to turn out as expected" for non-college-educated U.S. workers.[168]

97. As evidence of this larger "cumulative disadvantage" that reaches beyond wages and income, Case and Deaton (2017) point to a number of empirical facts relating to non-college-educated men and women. Labor force participation rates have declined for each successive male birth cohort since 1940.[169] Marriage rates are lower at any given age for each cohort born since 1945.[170] Relatedly, divorce rates are higher relative to college-educated men and women.[171] And childrearing outside of marriage has increased substantially, particularly for white, non-college-educated women.[172]

98. These changing social arrangements have consequences, according to the authors. "Unmarried, cohabiting partnerships are less stable than marriages," so "both men and women lose the security of the stable marriages that were the standard among their parents."[173] In addition, when children are born into these less stable, cohabiting relationships and the relationship does not stay intact, men often "lose regular contact with their children, which is bad for them, and bad for the children, many of whom live with several men during childhood."[174] Moreover, the process of several men entering and leaving the home can be difficult for both the

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[165] Case and Deaton (2017), pp. 429, 438–39.
[166] Case and Deaton (2017), p. 438.
[167] Case and Deaton (2017), p. 420.
[168] Case and Deaton (2017), pp. 429–30, 433–34, 438.
[169] Case and Deaton (2017), p. 430.
[170] Case and Deaton (2017), p. 431.
[171] Case and Deaton (2017), p. 431.
[172] Case and Deaton (2017), p. 432.
[173] Case and Deaton (2017), p. 431.
[174] Case and Deaton (2017), p. 432.

adults, who lose the stability and security of a more committed relationship, and the children, who see some men that are "unsuitable as fathers" and others who are "suitable," but "bring renewed loss … when it is their turn to depart."[175]

99. These are the effects on family, fulfillment, and perceptions of life's meaning and satisfaction that Case and Deaton (2017) are referencing when they note how an economic explanation alone is insufficient to explain "deaths of despair." Despair does not come only from lower real wages. It results from the accumulation of disadvantage stemming from shifts since the 1970s in more fundamental social and economic arrangements for non-college-educated men and women in the U.S. This cumulative disadvantage then leads to "increasing distress, and the failure of life to turn out as expected" for these individuals.[176] This in turn can lead people to "compensat[e] through other risky behaviors such as abuse of alcohol and drug use that predispose toward [negative] outcomes…"[177] Deaths stemming from these behaviors and suicides are "deaths of despair."[178]

100. In the comment he wrote on Case and Deaton (2017), Professor Cutler states that there is no way to understand the increase in mortality among non-college-educated U.S. individuals aged 45–54 "without considering the sources of despair, and the sources of despair must be very deep-seated indeed."[179] "At root," he says, "is economic and social breakdown."[180] Consistent with this, he agrees with Case and Deaton (2017)'s despair narrative:

> Their [Case and Deaton (2017)] overall suggestion is [that] [p]eople despair when their material and social circumstances are below what they had expected. This despair leads people to act in ways that significantly harm their health. This may have a direct impact on death through suicide, or an indirect impact through heavy

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[175] Case and Deaton (2017), p. 432.
[176] Case and Deaton (2017), p. 434.
[177] Case and Deaton (2017), p. 434.
[178] Other academics writing about the increase in drug overdoses in the U.S. in the past few years have cited Case and Deaton (2017) and this deep despair idea. For example, Jalal et al. (2018) noted that "sociological and psychological 'pull' forces may be operative to accelerate demand [for drugs], such as despair, loss of purpose, and dissolution of communities. Elucidation of the dynamics of these 'deep' drivers of the overdose epidemic may provide valuable new insights." Hawre Jalal et al., "Changing dynamics of the drug overdose epidemic in the United States from 1979 through 2016," *Science*, 361, no. 6408, 2018 ("Jalal et al. (2018)").
[179] Case and Deaton (2017), p. 445.
[180] Case and Deaton (2017), p. 445.

> drinking, smoking, drug abuse, or not taking preventive medications for conditions such as heart disease. At root is economic and social breakdown.
>
> This explanation is certainly correct.[181]

101. In line with this narrative, Professor Cutler recognizes that opioids are closer to symptoms rather than causes of the underlying despair. Curiously, however, even though Professor Cutler recognizes the importance of this multi-faceted, underlying despair that is so critical in explaining "deaths of despair," he makes no attempt in his direct regression model to account for many of the non-economic elements of the underlying despair. For example, he does not include marriage rates, cohabitation rates, out of wedlock birth rates, church membership and attendance, civic engagement, or union membership in his model.[182] This matters because if despair driven by changing societal norms causes opioid-related deaths, then failure to account for these factors will result in inflated estimates of the impact of prescription opioid shipments on mortality.

102. Part of the reason Professor Cutler may not have included such factors in his model is that, as Case and Deaton (2017) and Professor Cutler recognize, these factors are difficult to measure at the local level over extended periods of time and ultimately may not even sufficiently capture the hard-to-measure underlying despair.[183] But Professor Cutler does not appear to have made an effort to find a direct proxy for "despair." Instead, he simply says that he "controlled for as many factors as [he] could possibly get any information on…" and "… took account of everything that [he] could think of that would pick up the malaise [discussed by Case and Deaton (2017)]."[184]

103. Had he sought to more fully account for "despair," however, he might have discovered that there is in fact a proxy available which can be used to isolate, at least to some degree, the

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[181] Cutler comment on Case and Deaton (2017), p. 445. In his deposition, Professor Cutler agreed that "there is a lot of malaise in many parts of the country that would remain even without opioids." Deposition of David Cutler, April 26, 2019 ("Cutler Deposition"), 304:21–305:2.
[182] Cutler Report, ¶ 88 and Appendix III.H.
[183] Case and Deaton (2017), pp. 437, 445.
[184] Cutler Deposition, 305:11–17. Professor Cutler goes on to say that he "believe[s] that I have included many, many variables [in his regressions] that reflect the 'deep malaise' or the difficulty that people are feeling associated with economic conditions, social conditions, demographic conditions." Cutler Deposition, 312:14–313:5.

separate, incremental impact of prescription opioid shipments on mortality.[185] This proxy is the non-opioid-related "deaths of despair" rate, as measured by Case and Deaton (2015 and 2017).[186]

104. When one includes this despair proxy in Professor Cutler's direct regression model, the incremental impact of prescription opioid shipments on mortality falls substantially, while the impact of the despair is positive and statistically significant. Specifically, as shown in Exhibit 2, the estimated impact of prescription opioid shipments on opioid-related mortality per 100,000 people drops by more than half from [redacted] The model is also better able to explain the variation seen across counties in opioid-related mortality, indicating that underlying despair is an important factor in explaining the change in opioid-related mortality between 1993–1995 and 2009–2010.

105. Similarly, accounting for underlying despair reduces Professor Cutler's subsequent estimates of the share of opioid-related mortality attributable to Defendants' alleged misconduct based on his direct regression model. In particular, his estimates of the share of opioid-related mortality due to Defendants' alleged misconduct in each year from 2006 to 2010, which he shows in his Table III.10, fall from a range of [redacted] percent to a range of [redacted] percent, as shown in my Exhibit 3. Likewise, his estimates of the share of licit opioid-related mortality due to Defendants' alleged misconduct in each year from 2010 to 2016, which he shows in his Table III.11, fall from a range of [redacted] percent to [redacted] percent, as shown in my Exhibit 4.

[185] This incremental impact would include the extent to which prescription opioid shipments increase the likelihood that despair leads to death.

[186] The different types of "deaths of despair" Case and Deaton (2017) identify (alcoholism-related mortality, opioid-related mortality, other drug-related mortality, and non-drug-and-alcohol suicides) can be thought of as being driven by a common component (the "cumulative disadvantage," deep despair that is driving all "deaths of despair," and an idiosyncratic component specific to each type). Provided the idiosyncratic components are not highly correlated across the different types, non-opioid-related "deaths of despair" will be a good proxy for the common component, and can be used in a regression model focused on explaining opioid-related "deaths of despair" rate to account for this important factor that Professor Cutler omits from his model. I calculate "deaths of despair" rate according to Case and Deaton's method, using the same ICD-9 and ICD-10 codes as they do to isolate deaths resulting from drug overdoses, suicide, and alcohol-related liver mortality. To these codes, I add the ICD codes representing assault by drugs in order to make Case and Deaton's drug death definition consistent with Professor Cutler's. I then subtract Professor Cutler's opioid mortality rate from this "deaths of despair" rate to get non-opioid-related "deaths of despair" rate.

2. Indirect Regression Model

106. Professor Cutler implements two indirect regression models in order to estimate the impact of opioid shipments on opioid-related mortality. The first indirect regression model uses a baseline period of 2008–2010 to estimate illicit opioid-related mortality for the 2011–2016 period based on economic and demographic factors. The second indirect regression model uses a baseline period of 1993–1995 to estimate all opioid-related mortality for the 2006–2016 period based on economic and demographic factors.

107. Similar to Professor Rosenthal's indirect regression models, Professor Cutler's indirect regression models are flawed because they attribute any opioid-related mortality not explained by a limited set of economic and demographic factors to prescription opioid shipments. This is not a valid assumption. As Professor Cutler acknowledges in his report:

> The indirect regression attributes the entirety of unexplained opioid-related mortality to shipments. To the extent that other factors not modelled in the "baseline" regression contributed to increases in opioid mortality, the indirect approach has the potential to overstate the impact of defendants' actions.[187]

108. Hence, if there are any factors that contributed to the increase in opioid-related mortality that Professor Cutler does not model—either because they are hard to measure or because he does not think they warrant inclusion—then his indirect model admittedly inflates the impact of prescription opioid shipments. One such factor is the underlying "despair" I discussed above.[188] Professor Cutler does not attempt to model many of the non-economic elements of underlying despair in his indirect regression model.

109. Nor does he attempt to model how the availability, potency, and price of illicit opioids (*e.g.*, heroin, fentanyl) trafficked by drug dealers affect opioid-related mortality.[189] There is

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[187] Cutler Report, ¶ 78, FN 53.

[188] *See* Cutler comment on Case and Deaton (2017), p. 445 for evidence of Professor Cutler acknowledging the importance of "deaths of despair."

[189] Professor Cutler claims that "thicker" illicit opioid markets post-2010 were "partially a result of opioid shipments prior to 2010." *See* Cutler Report, ¶ 71. He provides no causal evidence for this claim, however; nor does Professor Gruber, to whom Professor Cutler cites. *See* Cutler Report, ¶ 71; Expert Report of Professor Jonathan Gruber, March 25, 2019 ("Gruber Report"), ¶ 66. Even if this were the case though, Professor Cutler would need to take into account any portion of the increased supply of illicit opioids that is not due to opioid shipments to produce accurate estimates of the share of opioid-related mortality caused by shipments. In addition, Professor Cutler fails to

evidence that the availability and potency of heroin increased and heroin prices fell after 2010.[190] This may have caused some individuals who were already abusers of drugs besides opioids to switch from these other drugs to heroin. Such a switch by a drug abuser would be unsurprising because most heroin users have used other, non-opioid drugs. Specifically, the NSDUH survey data show that 89 percent of all heroin users between 2002 and 2014 used an illicit substance or non-medically used a prescription substance besides pain relievers prior to using heroin. Excluding marijuana, the share is 74 percent, among whom 65 percent used cocaine prior to using heroin and 71 percent used hallucinogens prior to using heroin.[191] Similarly, Cicero et al. (2017) show that the share of individuals who started with heroin as their first opioid of abuse increased from 9 percent in 2005 to 33 percent in 2015, while the share of oxycodone as the initiating opioid dropped from 42 percent to 24 percent over the same time period.[192] To the extent any of these drug-abusing individuals started to use heroin as a result of changing supply or prices post-2010, and then later died of heroin-related causes, Professor Cutler's indirect model would incorrectly attribute their deaths to prescription opioid shipments.

110. Likely even more important is the emergence of illicitly manufactured fentanyl and its analogs (*e.g.*, carfentanil). Fentanyl and its analogs have caused opioid-related mortality to increase sharply since 2013—essentially making illicit opioid use deadlier. This can be seen by the increase in the ratio of mortality to misuse among illicit opioids. In both 2014 and 2016 this ratio increased by more than 30 percent over the prior year.[193] This increase impacts illicit

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recognize in his report that the opposite relationship between prescription opioids and illicit opioids might hold—*i.e.*, to the extent prescription opioids served as a substitute for illicit opioids, it is possible that illicit opioid markets were thinner than they would have otherwise been.

[190] *See*, *e.g.*, Jalal et al. (2018), p. 2, which notes that after 2010, heroin became "increasingly more available, [...] purer and less expensive than prescription opioids."

[191] Professor Cutler notes that among NSDUH respondents who reported using both heroin and prescription opioids for non-medical use, 83 percent reported using prescription opioids first. *See* Cutler Report, ¶ 62. Professor Cutler does not specify that the 83 percent refers to non-medical use, not just use generally. A more precise statement of this point, therefore, is that among NSDUH respondents who reported using both heroin and prescription opioids for non-medical use, 83 percent reported using the prescription opioids for non-medical use first. In this light, it is unsurprising that of this group of drug-abusing individuals, 81 percent also previously used another illicit substance or non-medically used another, non-pain-reliever prescription substance.

[192] Cicero et al., "Increased Use of Heroin as an Initiating Opioid of Abuse," *Addictive Behaviors*, Vol 74, 2017, pp. 63–66.

[193] To calculate the mortality rate due to illicit opioids, I use Professor Cutler's "illicit_rate2" variable from the "mortality_rates" file in his backup. This rate variable includes all deaths due to heroin and fentanyl. To estimate the rate of heroin or illicit fentanyl use, I use NSDUH data. In particular, I use the variable HEREVER, which indicates whether the respondent has ever used heroin, and all the variables that ask respondents about drugs they

opioid users overall, regardless of whether their illicit opioid use stemmed from pre-2010 prescription opioid shipments or not. Yet, because this increase will not be explained by Professor Cutler's indirect regression model, he attributes all of the increase to prescription opioid shipments. This severely biases upward his estimate of illicit opioid-related mortality caused by prescription opioid shipments. In sum, Professor Cutler apparently believes that all of the increase in the illicit opioid-related mortality rate is due to the reformulation of OxyContin and other policy changes surrounding licit opioids starting in 2010.[194] He does not consider the possibility of independent changes in supply conditions.

111. I have updated Professor Cutler's calculation of the share of illicit opioid-related mortality between 2011 and 2016 attributable to Defendants' alleged misconduct to partially address the flaws discussed above. These updates can be seen in Exhibit 5, which is an updated version of Professor Cutler's Table III.12. First, I have adjusted predicted mortality relative to 2010 to take into account changing heroin potency and the emergence of fentanyl and its analogs. This is accomplished by adding a column to Professor Cutler's Table III.12 that reflects the annual ratio of mortality to misuse among illicit opioids, relative to the ratio in 2010. I then multiply these numbers by Professor Cutler's "predicted mortality relative to 2010" to get a predicted mortality that incorporates the changing heroin potency and emergence of fentanyl. The second update I have made to the table is to account for despair in the indirect regression underlying column B. Third, I have incorporated the results of Professor Cutler's direct

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have ever injected. For the latter category, the question shifts from asking about injecting drugs not prescribed to you or only for the experience or feeling it caused from 2002–2014 to only injecting drugs not prescribed to you from 2015–2017. I use these injection variables because there is no single variable indicating whether a respondent has used illicit fentanyl. I then calculate the share of respondents in each year who have used heroin or injected fentanyl as the share of respondents who either answered affirmatively to the HEREVER question or listed fentanyl as a drug they injected that wasn't prescribed to them or, in the early period, only for the feeling or experience. Also due to the question change between 2014 and 2015, I estimate the 2015 ratio by applying the average percentage change in the ratio in the two adjacent years, 2014 and 2016, both of which had the same question asked in the prior year.

[194] Professor Cutler's opinion that OxyContin's reformulation in 2010 was one of the principal causes of the subsequent decline in the supply of prescription opioids and that this in turn caused an increase in the demand of illicit opioids is contradicted by Professor Rosenthal's results. Specifically, version C of Professor Rosenthal's direct model explicitly tests for the impact of OxyContin's reformulation on nationwide prescription opioid sales and finds no statistically significant impact. *See* Rosenthal Report, Table 1.

regression model that also accounts for despair, as shown in column 2 of Exhibit 2.[195] This last step changes the [redacted] percent impact for 2010 to [redacted] percent.

112. The results of these three limited updates alone show that Professor Cutler's illicit opioid-related "percent impact on mortality" calculations overstate the impact of prescription opioid shipments. In particular, my adjustments lower the percent impact from a range of [redacted] percent, as shown in the top panel of Exhibit 5, to a range of [redacted] percent, as shown in the bottom panel. Exhibit 6 then updates Professor Cutler's Table III.13, where Professor Cutler combines his estimates for the direct and indirect models and licit and illicit opioids before and after 2010 to provide his estimate of the overall share of opioid-related mortality attributable to Defendants' alleged misconduct under his Approach 1. My adjustments lower the overall percent impact from [redacted] percent (top panel) to [redacted] percent (bottom panel). Note that even these adjusted estimates are still inflated because they rely on Professor Rosenthal's fundamentally flawed and inflated estimates of the impact of Defendants' marketing on opioid shipments and the unsupported assumption that all of Defendants' marketing was unlawful. I present them only to show the fragility of Professor Cutler's model, not as an opinion as to an attributable percentage of responsibility.

113. Like Professor Rosenthal, Professor Cutler's use of the indirect approach is also flawed because he assumes that the relationships in the baseline period between the outcome he is trying to predict (in this case opioid-related mortality) and economic and demographic factors do not subsequently change. Under Approach 2, Professor Cutler's baseline period is 1993–1995 which means that Professor Cutler is assuming that the economic and demographic factors he includes in his indirect regression had the same relationship to opioid-related mortality in 1993–1995 as they had twenty years later. Yet the world has changed since 1995 in ways that are likely to alter these relationships. It is likely, for example, that widespread access to the Internet and the proliferation of cell phones and later smartphones has had an impact on the relationship between

[195] In Exhibit 5, I also correct Professor Cutler's mathematical error in his calculation of the average illicit opioid-related mortality rate. Specifically, Exhibit 5 calculates the average mortality rate as the average of the mortality rates across the 404 counties included in Professor Cutler's indirect regression. Professor Cutler mistakenly calculates the actual mortality rate as the exponential of the average of 404 counties' logarithms of their mortality rates. Because the exponential of an average of logarithms is not the same as the simple average of the observations' levels, this is incorrect. In this case, it produces mortality rates that are too low by [redacted] percent in each year, 2006–2016.

economic and demographic factors and opioid-related mortality by, for example, making it easier to obtain illicit drugs.[196] In addition, changing economic conditions have altered the economic consequences of having only a high school education versus a college education.[197] Professor Cutler's indirect regression models do not take any of these changing relationships into account.

114. Finally, Professor Cutler's 1993–1995 indirect regression model is also flawed because it fails to take into account pre-existing trends in opioid-related mortality during his baseline period, and how those trends may have impacted opioid-related mortality going forward. Such trends may be meaningful in helping explain subsequent movements in opioid-related mortality. The importance of taking pre-existing trends into account was recognized by Professor Rosenthal who accounts for a "secular trend" in her indirect regression model, and it has also been recognized in the published literature.[198] Professor Cutler, however, has done nothing to test for or incorporate prior trends in opioid-related mortality into his 1993–1995 indirect regression.[199]

115. Exhibit 7 shows what happens to Professor Cutler's predicted opioid-related mortality estimates for 1996 through 2016 under his Approach 2, which relies on his 1993–1995 indirect

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[196] A number of academic papers discuss how the proliferation of cell phones, then the Internet, and most recently social media have made it easier to obtain illicit drugs. For example, May and Hough (2004) describe how the spread of mobile phones "radically transformed retail drug markets" and "minimise[d] the risks associated with illicit transactions by making telephone surveillance largely impractical." Tiggey May and Mike Hough, "Drug Markets and Distribution Systems," *Addiction Research and Theory* 12, no. 6, December 2004, pp. 549–63 at p. 554. Similarly, Demant et al. (2018) discuss how more recently, "cryptomarkets" on the Internet such as Silk Road and Agora offer buyers and sellers of illicit drugs several advantages over offline drug purchases (*e.g.*, less risk of violence in the transaction, more security in the form of anonymity and encryption). Jakob Demant, Rasmus Munksgaard, and Esben Houborg, "Personal use, social supply or redistribution? Cryptomarket demand on Silk Road 2 and Agora," *Trends in Organized Crime* 21, no. 1, 2018, pp. 42–61 at pp. 43–45. And most recently, Moyle et al. (2019) point out that social media apps such as Snapchat, Instagram, and WhatsApp provide a valuable intermediary option for illicit drug buyers and sellers between cryptomarkets and street dealing—with "secure" features and "the opportunity to preview product without the requirement for technical expertise." Leah Moyle, Andrew Childs, Ross Coomber, and Monica Barratt, "#Drugsforsale: An exploration of the use of social media and encrypted messaging apps to supply and access drugs," *International Journal of Drug Policy* 63, 2019, pp. 101–10 at p. 101.

[197] Goldin, Claudia, and Lawrence Katz, "The Race between Education and Technology: The Evolution of U.S. Educational Wage Differentials, 1890 to 2005," NBER Working Paper No. 12984, March 2007, pp. 28–29.

[198] Rosenthal Report, ¶¶ 81, 87; Seema Jayachandran et al., "Modern Medicine and the Twentieth Century Decline in Mortality: Evidence on the Impact of Sulfa Drugs," *American Economic Journal: Applied Economics* 2, 2010, pp. 118–46 at p. 131; Quan Li and Ming Wen, "The Immediate and Lingering Effects of Armed Conflict on Adult Mortality: A Time-Series Cross-National Analysis," *Journal of Peace Research* 42, no. 4, 2005, pp. 471–92, p. 479; Peng Yin et al., "Particulate Air Pollution and Mortality in 38 of China's Largest Cities: Time Series Analysis," *BMJ* 356, no. 8097, 2017, pp. 2, 9.

[199] Professor Cutler could use the same NVSS mortality data he uses in his direct and indirect model analyses to incorporate this trend.

regression, when I relax two of his assumptions. In particular, I relax the assumptions that "despair" has no impact on opioid-related mortality and, contrary to Professor Cutler, I allow the trend in opioid-related mortality apparent in the baseline period (1993–1995) to continue after 1995.[200] The result is a predicted mortality rate that is much higher than Professor Cutler's predicted rate.[201] Over the 2006–2016 period, the adjusted predicted rate is between three and nine times higher than Professor Cutler's predicted rate. This substantially reduces the unexplained opioid-related mortality that Professor Cutler attributes to shipments. Taking into account the impact of heroin and fentanyl supply would reduce the unexplained opioid-related mortality even further. Exhibit 8 shows the impact of these two adjustments on Professor Cutler's Table III.14 where Professor Cutler provides his estimates of the overall share of opioid-related mortality attributable to Defendants' alleged misconduct under his Approach 2 between 2006 and 2016. My adjustments lower the overall percent impact from [redacted] (top panel) to [redacted] percent (bottom panel). Note again that these estimates are still inflated because they rely on Professor Rosenthal's fundamentally flawed and inflated estimates of the impact of Defendants' marketing on opioid shipments and the unsupported assumption that all of Defendants' marketing was unlawful.

B. Professor Cutler's Calculations of the Shares of Harm Attributable to Defendants' Alleged Misconduct

116. Professor Cutler's next step is to apply his Approach 1 and Approach 2 estimates of the impact of Defendants' alleged misconduct on opioid-related mortality to various other harms the Plaintiffs experienced that he claims are opioid related. After estimating what portion of government services in various divisions of Plaintiff County governments can be tied in some

[200] Exhibit 7 also uses simply the mortality rate rather than the logarithm of the mortality rate, as the outcome variable. This is because the time trend is assumed to have a linear relationship with the level, not the percentage change, of the annual opioid-related mortality rate. As pointed out by Professor Cutler, both forms of the dependent variable are used in the economics literature and by him. *See* Cutler Report, ¶ 89.

[201] Exhibit 7 also corrects Professor Cutler's mathematical error in his calculation of the average opioid-related mortality rate, as described above.

way to opioids,[202, 203] Professor Cutler assumes that opioid shipments have the same impact on other opioid-related harms as they have on opioid-related mortality.[204]

117. Professor Cutler provides two justifications for this assumption. First, he notes that comprehensive data across counties on opioid-related mortality are available, while this is not the case for the other harms. Of course, this tells us nothing about whether the assumption he makes is valid. His second justification is that in his view, there is a "direct connection between availability of legal and illegal opioids and opioid-related deaths" that is not present with the other types of harms.[205] But if that is true, then it suggests that the estimated impact of prescription opioid shipments may be greater for opioid-related mortality than the other harms because the impact on mortality is direct. In that case, applying estimates based on opioid-related mortality to other opioid-related harms leads to over-estimation of the impact of shipments on these harms.

118. Indeed, even were one to assume that opioid shipments have an incremental impact on opioid-related mortality after accounting for underlying despair, that does not mean that the same impact also exists for other types of harm. In his comment on Case and Deaton (2017), Professor Cutler expresses a concern with what he believes is overprescribing of opioids because "[h]eavy drinking and smoking can kill people, but it takes a long time. Addiction [to opioids] can kill much sooner. The net effect may thus be an increase in the extent to which despair can lead to death in the short term."[206] However, the same need not be true for other types of harm.

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[202] In his deposition, Professor Cutler suggested that he was not attempting to determine what share of harms were caused by opioids, but instead just the share that were related to opioids in any way. *See* Cutler Deposition, 212:1–213:5, 214:9–215:24, 254:18–255:3.

[203] Professor Cutler assumes opioid use disorder accounts for the same share of overall substance use disorder ("SUD") in juveniles as it does in adults in Ohio. However, according to the NSDUH data that Professor Cutler uses for this calculation, this is not correct. These data indicate that between 2006 and 2017, on average, opioid use disorder in Ohio accounted for 19.7 percent of juvenile SUD compared to 32.3 percent of adult SUD. This error causes Professor Cutler to inflate the share of juvenile criminal cases related to opioids by nearly 50 percent. (Note: In order to ensure privacy, NSDUH suppresses data when it concludes there would be fewer than 1,000 individuals that fall in a certain category at the state level. In instances where the number of minors who have exhibited heroin abuse or dependence within the past year is suppressed, 1,000 is inserted. Additionally, 19.7 percent is conservative since there exists a potential double-counting issue. This is because it is impossible to calculate the population of minors in Ohio who have both heroin abuse or dependence and pain reliever abuse or dependence due to the data limitations of the NSDUH portal.)

[204] Cutler Report, ¶ 47.

[205] Cutler Report, ¶ 47.

[206] Case and Deaton (2017), p. 451.

Heavy drinking (or other substance abuse), for example, can result in child maltreatment and/or crime in the short term.[207] As a result, after accounting for underlying despair, there may be no incremental impact of opioid shipments on certain types of crime—or other harms Professor Cutler has identified. Moreover, to the extent the non-mortality harms Professor Cutler identifies are driven by opioid use disorder ("OUD"), the differential growth in OUD rates and opioid-related mortality rates both before and after 2010 suggests further that the impact of shipments may be different for mortality than for other harms. Specifically, from 2002 to 2010, the OUD rate grew by 14 percent while the opioid-related mortality rate grew by 67 percent. The divergence then became even sharper from 2015 to 2017—with the OUD rate falling by 13 percent and the opioid-related mortality rate rising by 34 percent. Even with these differential growth rates, however, Professor Cutler assumes that his single estimate of the incremental impact of prescription opioid shipments on mortality applies to all other harms. There is simply no basis for this assumption.

119. To buttress this assumption that the impact of shipments on opioid-related mortality can be used more generally to estimate the impact of shipments on other opioid-related harms, Professor Cutler conducts what he refers to as a "supporting" analysis where he estimates the relationship between opioid shipments on two types of crime—property crime and violent crime.[208] Like his opioid-related mortality regressions, at the very least it is necessary to take into account underlying despair before concluding that prescription opioid shipments have an incremental impact on crime rates. When I update Professor Cutler's direct regression of violent crime to take into account despair, the association between violent crime and prescription opioid shipments is no longer statistically significant—*i.e.*, it is not statistically distinguishable from zero.[209] This result confirms that the incremental impact of opioid shipments, if any, is likely to vary across different types of harms. As a result, Professor Cutler's assumption that the impact

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[207] Isabel Wolock and Stephen Magura, "Parental Substance Abuse as a Predictor of Child Maltreatment Re-Reports," *Child Abuse & Neglect* 20, no. 12, 1996, pp. 1183–93 at p. 1190; Kelly Kelleher et al., "Alcohol and Drug Disorders among Physically Abusive and Neglectful Parents in a Community-Based Sample," *American Journal of Public Health* 82, no. 10, 1994, pp. 1586–1590 at p. 88; Lawrence A. Greenfeld, "Alcohol and Crime: An Analysis of National Data on the Prevalence of Alcohol Involvement in Crime," U.S. Department of Justice Report No. NCJ 168632, April 28, 1998.

[208] Cutler Report, ¶¶ 124–133 and Appendix III.L.

[209] After taking into account underlying despair, the relationship between shipments and property crime is smaller in magnitude, but remains statistically significant.

of shipments on opioid-related mortality can serve as a proxy for the impact of shipments on other opioid-related harms is wrong and renders his estimates unreliable.

VI. Review of Professor McGuire's Damages Analysis and Opinions

120. Professor McGuire's damages report consists of four broad opinions. First, he outlines what he contends is a valid economic framework to calculate damages to Plaintiffs attributable to Defendants' alleged misconduct. Second, he claims to identify certain divisions of the Plaintiff County governments that were affected by the opioid epidemic from 2006 to 2018. Third, he claims to identify those costs affected by the opioid epidemic within these Plaintiff County government divisions. Finally, he estimates damages accruing from 2006 to 2018 to Cuyahoga and Summit Counties due to Defendants' alleged misconduct. Professor McGuire's opinion is not based on evidence that the Plaintiffs incurred damages due to Defendants' alleged misconduct. Rather he relies on either isolated anecdotes or entirely hypothetical assertions. I detail below the flaws in his methodology that render his opinions unreliable.

A. Professor McGuire's Economic Framework to Calculate Damages

121. Professor McGuire alleges that Defendants' alleged misconduct led to excessive shipments which in turn increased harms to residents of the Plaintiff Counties, and that addressing these harms led to costs to the Plaintiffs.[210] As Professor McGuire conceded in his deposition, errors in the analyses of Professors Rosenthal and Cutler necessarily impact his analyses because Professor McGuire adopts the share of opioid-related harms due to Defendants' alleged misconduct from Professor Cutler, which in turn relies on results from Professor Rosenthal.[211] As discussed in Sections IV and V, the analyses of Professors Rosenthal and Cutler suffer from critical methodological errors. As a consequence, Professor McGuire's damages estimates are severely inflated, even if there were no other flaws or errors in his analysis.

[210] McGuire Damages Report, ¶ 14.
[211] Deposition of Thomas McGuire, April 23, 2019 ("McGuire April 23 Deposition"), 143:17–146:15, 205:14–19.

B. Professor McGuire's Opinion Regarding Resource Reallocation in Plaintiff Counties Government Divisions

122. Professor McGuire invokes the economic concept of "opportunity cost" to suggest that any resources expended on opioid-related services are damages even if they did not increase the overall costs to the Counties.[212] He explains that such costs came at the expense of other services and notes that the "reallocation of resources is the cost of providing Bellwether Government services in response to the opioid crisis."[213] Professor McGuire does not show, however, that the provision of opioid-related services by the Plaintiffs has caused a reallocation of resources. His opinion that such a reallocation has occurred specifically in the Plaintiffs is based solely on the deposition of Summit County official, Greta Johnson.[214] While Ms. Johnson provides single instances of alleged resource reallocation, her examples do not cover Cuyahoga County at all, nor do they cover all of the Summit County divisions included in Professor McGuire's damages estimate. Ms. Johnson is also unable to quantify services in Summit County that were formerly allocated for other uses but diverted to address opioid-related harms.[215]

123. Depositions from a number of additional fact witnesses suggest limited evidence that any such reallocation of resources has actually happened to any economically significant extent. Many Plaintiff County officials put forth as witnesses by Plaintiffs testified to a limited or undetectable impact of opioid use and abuse on the County, and note that they are unaware of any quantification of the alleged impact. The Chief Investigator of the Summit County Medical Examiner's Office and the Director of the Cuyahoga County Office of Budget Management state that they only began to notice financial impacts attributable to opioids in their departments

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[212] McGuire Damages Report, ¶¶ 27–29, FN 26.
[213] McGuire Damages Report, ¶ 24.
[214] McGuire Damages Report, ¶ 29. Professor McGuire also provides examples of alleged reallocation in the governments of two cities, but he fails to justify why impacts to other parties are relevant to allegations of harm by the Plaintiffs. Specifically, he references a news article regarding police resources in the City of Tallmadge. He then indicates there are "numerous examples of such diversion outside of the Bellwether government divisions," citing only the deposition of Gary Gingell of the Cleveland Division of Police.
[215] Deposition of Greta Johnson, January 15, 2019, 198:5–201:5. A minor exception might be that Ms. Johnson notes that the Summit County medical examiner's office lost a stream of revenue because the office was no longer able "to perform several autopsies for outside agencies for cost." Her other examples of programs that have lost resources consisted only of qualitative descriptions. In other cases, she speculated regarding several programs that might have had more funding or resources but for the need to address opioid-related harms, but it does not appear these funds were formally allocated for another activity.

starting in 2015, nearly a decade after the start of Professor McGuire's damages calculations.[216] Specifically, when asked "2015 is the first year when you're comfortable saying that Cuyahoga County experienced specific financial impacts related to the use and abuse of opiates," Margaret Keenan, the Director of the Cuyahoga County Office of Budget Management responded "[t]hat's correct."[217]

124. Even when Plaintiffs' witnesses claim they had to reallocate or increase resources, they are unable to quantify the impact on resources due to opioid-related harms with any specificity. For instance, out of three different Plaintiffs' witnesses, two stated costs associated with their department increased significantly around 2015 and 2016, but admitted they didn't know how much of that increase was due to opioids.[218] The third, Lisa Kohler, the Chief Medical Examiner in Summit County, admitted she did not know the cost to her office due to the misuse of prescription opioids over time, nor due to illicit drugs as a whole.[219] Given the magnitude of diverted resources implied by Professor McGuire's large damages estimates, one would think it would be feasible to quantify the services foregone and their costs.

125. Resource reallocation may not be required if a division has excess capacity. Professor McGuire argues that government divisions may need excess capacity to deal with occasional unpredictable periods of high demand,[220] but he has not demonstrated that such periods of high demand ever occurred during the time period of interest. Indeed, he does not seek to measure the capacity utilization levels of the relevant divisions of Plaintiff County governments during any time period in his analysis. Moreover, one may find that seemingly fully utilized staff become more efficient as demands on their time increase. If an existing government employee is able to address opioid-related activities without loss of attention to other services and activities, then his

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[216] Deposition of Margaret Keenan, December 12, 2018 ("Keenan Deposition"), 370:21–371:2; Deposition of Gary Guenther, October 16, 2018 ("Guenther Deposition"), 200:2–17.
[217] Keenan Deposition, 370:21–371:2.
[218] Guenther Deposition, 200:2–17; Deposition of Cynthia Weiskittel, November 13, 2018, 90:12–25.
[219] Deposition of Lisa Kohler, July 31, 2018, 378:23–379:19. (Q. "Do you know how much your office spends per year as a result of the misuse of prescription opioids? …" A. "No, sir." Q. "Do you know how that figure has changed over time? …" A. "No, sir." Q. "Do you know the cost to your office on an annual basis as a result of illicit drug use?" A. "No, sir."
[220] McGuire Damages Report, ¶¶ 32–34.

or her efforts toward opioid-related activities do not constitute damages from an economic perspective.

C. Professor McGuire's Opinion on the Plaintiff County Government Divisions Affected by the Opioid Crisis and Associated Costs

126. Professor McGuire identifies Plaintiffs' "costs of providing services attributable to the opioid [crisis]" in two steps.[221] First, he identifies the divisions of Plaintiff County governments most impacted by the opioid crisis through review of division budget and expenditure information, activities, and interviews with local officials.[222] He also provides examples of resources expended in relation to harms that involved opioids in the Plaintiff Counties.[223] Aside from this information, Professor McGuire provides little insight into how affected divisions were identified.

127. Second, Professor McGuire identifies cost categories within each division that could have been affected by the opioid crisis based on a review of Plaintiffs' expenditure data from 2006 to 2018 and interviews with local officials.[224] He notes that cost categories must be "'variable' in the sense that they move up or down as the composition of the service provided by each division changes."[225] It is unclear how Professor McGuire used interviews to inform this process. The list of interviewees in Professor McGuire's report only includes officials from the City of Cleveland. In deposition, Professor McGuire noted that about 40 discussions with Plaintiff personnel were conducted by his staff,[226] but no notes taken during these discussions have been produced by Professor McGuire to confirm their content or allow a review of his interpretation of them. Although he provides budget data and his classifications, Professor McGuire does not provide sufficient information to evaluate whether a robust, scientific methodology was

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[221] McGuire Damages Report, ¶ 25.
[222] McGuire Damages Report, ¶ 51. In addition, Professor McGuire conceded in his deposition that he did not conduct these interviews and instead relied upon his staff to conduct them. McGuire April 23 Deposition, 73:2–81:13.
[223] McGuire Damages Report, ¶¶ 41–50.
[224] McGuire Damages Report, ¶ 58. He includes budget line items under the category of "compensation costs," such as salaries and benefits to compensate personnel, and "non-compensation costs" such as vehicles and maintenance expenses. McGuire Damages Report, ¶ 59.
[225] McGuire Damages Report, ¶ 56.
[226] McGuire April 23 Deposition, 74:9–74:18.

employed to identify variable costs in Cuyahoga and Summit County divisions. Indeed, during his deposition, Professor McGuire was unable to provide a clear description of the criteria and process used to categorize affected divisions and affected costs within those divisions.[227]

128. Further, Professor McGuire contends that for his damages calculation, it is sufficient to estimate Plaintiff expenditures on opioid-related activities.[228] He therefore does not assess whether the Plaintiff Counties efficiently used resources directed towards opioid-related services. That is, he does not assess whether the amounts paid were reasonable for the services delivered, a particular concern given the corruption scandals that have plagued Cuyahoga County.[229]

D. Professor McGuire's Opinion on Damages to the Plaintiffs Due to Defendants' Alleged Misconduct

129. To estimate damages to Plaintiffs, Professor McGuire multiplies the total expenditures of Plaintiff County government divisions potentially affected by the opioid crisis by Professor Cutler's estimates of the share of division costs due to Defendants' alleged misconduct.[230] The proper assessment of economic damages requires measuring the difference between the actual outcome and the outcome that would have occurred but for any alleged wrongdoing. From an economic perspective, harm that would have occurred regardless of any alleged wrongdoing cannot be considered economic damages because Defendants' alleged misconduct did not cause such harm. Yet nowhere in Professor McGuire's report does he directly analyze the impact of Defendants' alleged misconduct—or even of the opioid crisis in general—on Plaintiffs' costs.

130. In place of such an analysis, Professor McGuire relies on Professor Cutler's estimated share of harms to residents of the Plaintiff Counties due to Defendants' alleged misconduct. The share of harms due to Defendants' alleged misconduct is a poor proxy for the share of Plaintiffs'

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[227] McGuire April 23 Deposition, 117:15–129:7, 292:14–307:22. For example, during his deposition, Professor McGuire indicated that certain cost items required further confirmation through discussion with Plaintiff County officials or with his economics team to categorize these items as variable versus fixed costs. When asked to reconstruct which items needed confirmation, Professor McGuire stated "it's hard for me to think how one would reconstruct that beyond talking to the people."

[228] McGuire April 30 Deposition, 562:4–563:16.

[229] "Who's who of Cuyahoga County investigation," *Cleveland.com*, February 27, 2019, https://expo.cleveland.com/news/g66l-2019/02/5ece10a1647128/whos-who-of-cuyahoga-county-corruption-investigation- html, accessed on May 9, 2019; "Cuyahoga County's corruption investigation: a comprehensive guide," *Cleveland.com*, September 9, 2010, https://www.cleveland.com/countyincrisis/2010/09/schemes_title_to_come.html, accessed on May 9, 2019.

[230] The opioid-related share of division activities are provided in Cutler Report Tables III.4–III.8. The share of opioid-related harms due to Defendants' alleged misconduct are provided in Cutler Report Table III.13.

costs due to Defendants' alleged misconduct across divisions for at least two reasons. First, use of such a proxy relies upon the assumption that each additional opioid-related harm will lead the Plaintiffs to incur additional costs or reduce the provision of other valuable services as resources are diverted to address the opioid crisis. As discussed above, this need not be the case.

131. Second, Professor McGuire's application of Professor Cutler's estimated share of harms due to Defendants' alleged misconduct adopts Professor Cutler's assumption that the share of opioid-related harms in each Plaintiff County government division due to Defendants' alleged misconduct is adequately represented by Professor Cutler's estimate for the share of opioid-related mortality due to Defendants' alleged misconduct. As discussed in Section V, there is no basis for this assumption.

132. Further, Professor McGuire presents no methodology for allocating damages among the different types of Defendants such as manufacturer and distributor Defendants, nor among individual Defendants within each type. There is substantial variation among Defendants in the size and the nature of their business. Notably, Purdue's products accounted for only 2.9 percent of opioid prescriptions and 10.4 percent of opioid MMEs sold in the U.S. during the 2006–2018 damages period that Professor McGuire examines. In recent years, Purdue's share has been even lower. In 2018, Purdue's products accounted for only 2.4 percent of opioid prescriptions and 5.8 percent of opioid MMEs sold in the U.S.[231] Heterogeneity between Defendants' products and businesses would require some economically well-founded method for apportioning damages, yet Professor McGuire offers none.

133. Relatedly, Professor McGuire does not explore the role in the opioid crisis of hydrocodone products and the designation of these products as Schedule III controlled substances by the U.S. Drug Enforcement Administration ("DEA") until October 2014 or the upscheduling of them from 2014 forward.[232] Hydrocodone products have been on the market for

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[231] OxyContin's shares show similar patterns. Between 2006 and 2018, OxyContin accounted for 2.6 percent of prescriptions and 10.2 percent of MMEs in the U.S. In 2018, OxyContin accounted for 2.2 percent of prescriptions and 5.7 percent of MMEs. These figures are based on Professor Rosenthal's IQVIA data, which extend through May 2018. According to IQVIA patient count data, patients receiving OxyContin prescriptions as a share of all U.S. patients receiving opioid prescriptions was even smaller, ranging between 0.4 percent in 2006 to a peak share of 1.7 percent in 2009, after which the share steadily declined to only 0.9 percent in 2017.

[232] U.S. Drug Enforcement Administration Press Release, "DEA to Publish Final Rule Rescheduling Hydrocodone Combination Products," August 21, 2014.

over 75 years and largely consist of generic immediate-release combination products, accounted for 59 percent of opioid prescriptions and 27 percent of MMEs nationally from 2006 to 2018.[233] During the period from 2006 to 2017, 52 percent to 65 percent of patients obtaining opioid prescriptions obtained prescriptions for hydrocodone.[234] National NSDUH estimates indicate that during 2002–2014, nonmedical users of hydrocodone products accounted for between 47 and 69 percent of all nonmedical users of prescription pain relievers. From 2015 to 2017, the percentage of people who misused hydrocodone in each of these years was between 57 and 60 percent of all people who misused prescription pain relievers during those same years. The DEA moved hydrocodone combination products to Schedule II in October 2014 in response to this problem,[235] thereby imposing additional restrictions on the prescribing of these products.[236] For example, all prescriptions of Schedule II products must be written rather than called into the pharmacy and refills are not allowed.[237] Dr. Andrew Kolodny, the founder and Executive Director of Physicians for Responsible Opioid Prescribing, the organization that had petitioned the FDA in 2013 proposing increased restrictions on the use of opioids for chronic pain,[238] testified at the United States Senate Caucus on International Narcotics Control that had the DEA rescheduled these products in 2004, "thousands of overdose deaths and tens of thousands of cases of opioid addiction might have been prevented."[239]

134. In summary, Professor McGuire does not use rigorous scientific methods to identify Plaintiff County government divisions or the costs within these divisions that could have been impacted by the opioid crisis, nor does he use reliable methods to determine the damages to these divisions due to Defendants' alleged misconduct.

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[233] These figures are based on Professor Rosenthal's IQVIA data, which extend through May 2018.
[234] IQVIA patient count data.
[235] U.S. Drug Enforcement Administration Press Release, "DEA to Publish Final Rule Rescheduling Hydrocodone Combination Products," August 21, 2014.
[236] Office of Diversion Control, "Practitioner's Manual: An Informational Outline of the Controlled Substances Act," U.S. Drug Enforcement Administration Report, 2006.
[237] Office of Diversion Control, "Practitioner's Manual: An Informational Outline of the Controlled Substances Act," U.S. Drug Enforcement Administration Report, 2006.
[238] FDA letter to Andrew Kolodny, September 10, 2013.
[239] Andrew Kolodny, "America's Addiction to Opioids: Heroin and Prescription Drug Abuse," Statement for the Record before the Senate Caucus on International Narcotics Control, May 14, 2014, p. 4.

VII. Review of Professor McGuire's Public Nuisance Analysis and Opinions

135. In his report, Professor McGuire asserts that prescription opioid shipments constituted a public nuisance to the Plaintiff Counties based on the following opinions:

a. Shipments significantly interfered with public health, safety, peace, and comfort of members of the Plaintiff Counties with continuing and long-lasting effects;
b. The interference from shipments was unreasonable; and
c. Defendants were or should have been aware of the interference.[240]

He then attempts to quantify the economic cost of the alleged nuisance in six categories: mortality, morbidity, crime, child maltreatment, babies with neonatal abstinence syndrome ("NAS"), and Plaintiffs' costs. As discussed in more detail below, each of these opinions, as well as the quantification of the economic costs, are predicated on flawed assumptions and flawed estimates, and thereby invalidate Professor McGuire's analysis.

A. Professor McGuire's Opinion that the Shipments Significantly Interfered with Public Health, Safety, Peace, and Comfort

136. Professor McGuire's opinion that prescription opioid shipments significantly interfered with public health, safety, peace, and comfort depends crucially on Professor Cutler's analysis that purportedly establishes that shipments had a substantial impact on mortality and on Professor Cutler's assumption, also adopted by Professor McGuire, that shipments had the same substantial impact on other harms as they purportedly did on mortality. For harms such as crime and children placed in foster care, Professor McGuire also adopts Professor Cutler's estimate for what share of these harms are purportedly opioid related. For other harms, such as morbidity and NAS, as well as a broader definition of harm to children, Professor McGuire performs his own assessment of what share of these harms are purportedly opioid related, and then again following Professor Cutler's lead, assumes that shipments had the same substantial impact on these harms as they purportedly did on mortality.[241]

137. To begin with, as discussed in Section V, Professor Cutler's analysis of the impact of prescription opioid shipments on mortality is conceptually flawed. It overstates substantially the impact of shipments on mortality and fails to establish conclusively that the relationship between

[240] McGuire Public Nuisance Report, ¶ 38.
[241] McGuire Public Nuisance Report, ¶ 42.

them is causal, rather than merely an association, driven by other factors that impact both opioid shipments and mortality. Indeed, Professor McGuire himself never explains what size of an impact is necessary to meet the criterion of a "significant" interference.[242] Professor McGuire offers no independent analysis to demonstrate that shipments did interfere "significantly," or even at all, with "public health, safety, peace, and comfort" in the Plaintiff Counties, relying completely on Professor Cutler's flawed analysis to establish a causal link between shipments and any harms.[243]

138. Further, Professor McGuire's estimates include harms purportedly due to all shipments of opioids, not just those produced by manufacturer Defendants or associated with Defendants' allegedly unlawful marketing. Setting aside all the flaws in Professor Rosenthal's analysis discussed in Section IV, even she does not claim that all prescription opioid shipments were caused by Defendants' alleged misconduct. Indeed, Professor Rosenthal identifies some "clinically justifiable" uses of opioids and Professor McGuire, as discussed below, adopts this definition.[244] Yet, when claiming that prescription opioid shipments caused "significant" interference with "public health, safety, peace, and comfort" in the Plaintiff Counties, Professor McGuire fails to acknowledge that some of this so-called interference consists of shipments of prescription drugs for "clinically justifiable" uses.[245] Professor McGuire also does not separately identify the impact for either manufacturer or distributor Defendants. As discussed in Section VI, Purdue's share of shipments since 2006 (the period over which Professor McGuire calculates harms) was relatively small, particularly when measured in terms of number of prescriptions or number of individual patients.

139. Lastly, Professor McGuire fails to establish that prescription opioid shipments had any impact, significant or otherwise, on any of the other four types of harms he considers apart from mortality. Instead, he simply follows Professor Cutler's lead in assuming that opioid shipments had the same impact on all other types of opioid-related harms as they purportedly did on opioid-related mortality. Setting aside the flaws in Professor McGuire's methodology for estimating the

[242] McGuire Public Nuisance Report, ¶ 38.
[243] McGuire Public Nuisance Report, ¶ 38.
[244] Rosenthal Report, Section X; McGuire Public Nuisance Report, ¶ 63.
[245] McGuire Public Nuisance Report, FN 57.

share of these other harms that are opioid related (discussed in further detail below), there is no basis for assuming the same impact across all opioid-related harm categories.

140. In sum, Professor McGuire's opinion that shipments "significantly interfered with public health, safety, peace, and comfort" in the Plaintiff Counties is predicated both on Professor Cutler's flawed analysis and Professor McGuire's own flawed assumptions, with the result that both sets of flaws invalidate the reliability of this opinion.

B. Professor McGuire's Opinion That the Alleged Interference Was Unreasonable

141. Professor McGuire asserts that the alleged interference was unreasonable based on two opinions: (1) "the vast majority – at least [redacted] in Cuyahoga and at least [redacted] in Summit – of shipments to the Bellwether communities [from 2006 through 2016] were not justified by clinical need"[246] and (2) the costs of opioids outweigh their benefits.[247] As described in more detail below, both opinions are based on flawed and/or unreliable assumptions that are contradicted by the actions of relevant industry regulators and market participants.

1. Share of Opioid Shipments for "Clinically Justified" Uses

142. Professor McGuire's opinion that the large majority of shipments into the Plaintiff Counties were not for clinically justifiable uses rests on the assumption used by Professor Rosenthal that the only "clinically justified" uses of opioids are for end-of-life cancer pain and acute pain following surgery or trauma.[248] In other words, like Professor Rosenthal, Professor McGuire assumes that chronic pain cannot be appropriately treated with opioids. As discussed in Section IV, this assumption contradicts the FDA-approved label, as well as the actions of the FDA, the government authority charged with "protecting the public health by assuring the safety, effectiveness, quality, and security of human and veterinary drugs…"[249] It also contradicts the actions of the CDC (with respect to its guideline for opioids for chronic use), CMS and State

[246] McGuire Public Nuisance Report, ¶ 70.
[247] McGuire Public Nuisance Report, ¶¶ 71, 89.
[248] Rosenthal Report, Section X.
[249] "FDA Fundamentals," FDA, February 9, 2018, https://www fda.gov/about-fda/fda-basics/fda-fundamentals, accessed May 6, 2019.

Medicaid agencies (with respect to coverage and reimbursement of only therapies that are "reasonable and necessary" or "medically necessary"), private insurers and Plaintiffs themselves (with respect to reimbursement), and physicians (with respect to prescribing).[250]

143. Professor McGuire's assumption that chronic pain cannot be a "clinically justifiable" use is also contradicted by at least one of Plaintiffs' own clinical experts.[251] If that assumption is wrong, none of Plaintiffs' experts demonstrates that the chronic pain population is not large enough to more than account for the number of opioid MMEs shipped into the Plaintiff Counties.[252]

144. In addition to relying on Professor Rosenthal's analysis of "clinically justifiable" uses, Professor McGuire also relies on Professor Gruber's analysis as an additional support for his opinion that only a small portion of prescription opioid shipments to the Plaintiff Counties were for appropriate uses. Specifically, Professor McGuire notes Professor Gruber's finding that demographic and socioeconomic factors explain a small share of the variation in prescription opioid shipments across counties and cites to Professor Gruber's opinion that this "'suggest[s] that prescription activity, which drives shipments to an area, bears little relationship to medical need.'"[253] However, Professor McGuire fails to note that Professor Gruber's analysis of county-level prescription opioid shipments accounts for an even more limited set of explanatory variables than Professor Rosenthal's indirect model, despite apparently serving the same purpose. Specifically, while Professor Rosenthal's model accounts for certain healthcare characteristics, such as the number of cancer deaths per capita and the percent of uninsured residents in a county, Professor Gruber's model omits them altogether.[254]

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[250] Under Section 1862(a)(1)(A) of the Social Security Act, Medicare does not reimburse for any items or services that are not "reasonable and necessary." *See* "Medicare Program; Revised Process for Making Medicare National Coverage Determinations," *Federal Register* 68, no. 187, September 26, 2003, pp. 55634–41 at p. 55636; "Medicaid Documentation for Medical Professionals," Department of Health and Human Services and CMS Fact Sheet, December 2015; CDC 2016 Guideline, pp. 1–49. To the extent required by state, Medicaid programs also only cover medical necessities; in particular, under the Ohio Administrative Code 5160-1-01 and 5160-1-02, the state of Ohio rules that only services that are "medically necessary" can be reimbursed, and "[m]edical necessity is a fundamental concept underlying the Medicaid program." *See* "5160-1-02 General Reimbursement Principles," *LAWriter*, August 1, 2016, codes.ohio.gov/oac/5160-1-02v1, accessed May 6, 2019; "Chapter 5160-1 General Provisions," *LAWriter*, codes.ohio.gov/oac/5160-1, accessed May 6, 2019.

[251] Alexander Deposition, 31:24–32:6.

[252] Whether this is the case depends on the average length of treatment and average MMEs per day for patients suffering from chronic pain.

[253] McGuire Public Nuisance Report, ¶ 69.

[254] Rosenthal Report, Table 4; Gruber Report, Appendix I.D.

145. Additionally, Professor Gruber's model suffers from the same flaws as Professor Rosenthal's indirect model. As explained in Section IV, such indirect models fail to control for a number of other factors that would be expected to cause variation in prescription opioid shipments across counties, and more generally cannot be properly used to attribute the portion of the variation in opioid shipments across counties that remains unexplained by the model to any single factor such as Defendants' alleged misconduct. Lastly, Professor Gruber provides no assessment of what the appropriate level of shipments should be—for any of the counties he analyzed or the two Plaintiff Counties specifically. Variation in shipment levels across counties could mean that some counties are receiving too few shipments, rather than some counties receiving too many. In short, Professor Gruber's analysis is so limited in nature that it provides no support for Professor McGuire's claim that there were excessive shipments of prescription opioids into the Plaintiff Counties.

2. Costs and Benefits of Prescription Opioids

146. Professor McGuire opines that the interference of opioid shipments was unreasonable because the costs of prescription opioids outweigh their benefits measured in terms of quality-adjusted life years ("QALYs") and work force participation and productivity.[255]

Quality-Adjusted Life Years

147. To reach his opinion that the costs of prescription opioids outweigh their benefits in terms of impacts on QALYs, Professor McGuire compares the total person-days of OUD purportedly due to prescription opioids shipped to the Plaintiff Counties in 2014 to what he purports is the maximum possible person-days of "clinically justified pain relief" from opioids in these Counties.[256] Professor McGuire's comparison is flawed because he inflates estimates of OUD days caused by shipments and severely understates the number of pain relief days from opioid

[255] McGuire Public Nuisance Report, ¶ 89. As Professor McGuire explains, "QALYs assign a utility weight between 0 (death) and 1 (perfect health) to each year of life living in a certain state of health or illness. QALYs standardize utility into a single index that can be 'added up' across people." McGuire Public Nuisance Report, ¶ 83.
[256] McGuire Public Nuisance Report, ¶¶ 79–80.

use. As a result, his analysis of the impact of opioid use on QALYs lacks validity and his opinion is unreliable.

148. With respect to pain relief days, Professor McGuire's analysis is once again restricted to pain relief from the "clinically justified" uses assumed by Professor Rosenthal, and thus excludes the chronic pain population.[257] Setting aside other methodological problems with Professor McGuire's analysis, if it is clinically justifiable to use opioids to treat chronic pain, then only a fraction of the chronic pain population would need to be treated with opioids for pain relief days to outweigh OUD days. For example, if opioid treatment provides pain relief for an average of 90 days per year for chronic pain patients, the benefits of opioid shipments would outweigh their costs under Professor McGuire's methodology as long as approximately 29 percent of those suffering from chronic pain in the Plaintiff Counties received opioid treatment.[258] This percentage would be even lower if opioid treatment for the "clinically justified" uses outlined by Professor Rosenthal are included in the calculation. Thus, Professor McGuire's exclusion of chronic pain—a diagnosis that continues to be an FDA-approved indication—leads to an understatement of the benefits of opioid treatment.[259] Relaxing this assumption undermines his opinion that the costs of OUD caused by opioid shipments outweigh the benefits of pain relief.

149. With respect to Professor McGuire's estimate of OUD days, he estimates the number of people with OUD in 2014 due to shipments by first estimating the OUD population in the Plaintiff Counties and then multiplying this OUD population by Professor Cutler's estimate of the share of opioid-related harms due to shipments.[260] He then assumes that the OUD population in 2014 suffered from OUD for the entire year (365 days). Each step of this calculation is flawed and serves to inflate the number of OUD days.[261]

150. First, Professor McGuire overestimates the total OUD population in the Plaintiff Counties. Specifically, his estimated OUD rate of 1.5 percent of the population 12 years or older

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[257] Rosenthal Report, ¶ 92; McGuire Public Nuisance Report, ¶ 83.
[258] This calculation uses estimates of chronic pain prevalence from CDC. *See* James Dahlhamer et al., "Prevalence of Chronic Pain and High-Impact Chronic Pain among Adults – United States, 2016," *CDC Morbidity and Mortality Weekly Report* 67, no. 36, September 14, 2018, pp. 1001–6.
[259] FDA OxyContin Label, April 2014, PPLP003275296–307 at 296; Letter from FDA to Physicians for Responsible Opioid Prescribing, "Re: Docket No. FDA-2012-P-0818," September 10, 2013, p. 1.
[260] McGuire Public Nuisance Report, Appendix D.
[261] McGuire Public Nuisance Report, ¶ 80, FN 110.

is the sum of the rates of prescription OUD (0.9 percent) and heroin use disorder (0.6 percent), and thus double counts individuals exhibiting concurrent prescription opioid and heroin use disorder.[262] Professor McGuire also uses unfounded and unreliable assumptions to scale up NSDUH rates of prescription OUD (0.7 percent) and heroin use disorder (0.2 percent) to account for NSDUH's omission of the institutionalized and homeless populations.[263] For prescription OUD, Professor McGuire adopts estimates from Pitt et al. (2018), who adjust NSDUH rates of prescription OUD based on the number of prescription opioid-related deaths and an unsupported assumption that the risk of overdose death from severe prescription OUD is half the risk of overdose death from severe heroin use disorder.[264] Pitt et al. (2018) note that they make this *ad hoc* assumption because no reliable data exists on the risk of overdose death from severe prescription OUD. For heroin use disorder, Professor McGuire scales up NSDUH's rate based on a RAND study, in which the authors note that "[i]t is difficult to estimate the total number of heroin [chronic drug users] with great precision."[265] Indeed, the authors estimate a lower bound and an upper bound based on the uncertainty around a single parameter, and find that their estimate could be as much as 47 percent lower or 73 percent higher.[266] Professor McGuire thus employs unsupported or at best weakly supported assumptions without attempting to measure the uncertainty this introduces to his estimates of OUD days.

151. Second, as I described above, Professor Cutler's estimate of the size of the relationship between opioid shipments and opioid-related mortality (used as a proxy by Professor McGuire for the impact of shipments on OUD) is severely inflated, which in turn causes Professor McGuire's estimate of OUD days to be severely inflated.

152. Lastly, to calculate person-days of OUD, Professor McGuire assumes that individuals with OUD in 2014 have the condition for the entire year, which is the maximum possible number

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[262] Professor McGuire derives his prescription OUD prevalence estimate by scaling up opioid-related deaths that do not involve illicit opioids in an apparent attempt to try to avoid double counting individuals who suffer from both prescription OUD and HUD. Yet, this approach fails to resolve the double-counting issue. Instead, it simply assumes without any basis that individuals who suffer from HUD cannot subsequently die of a prescription opioid overdose where no heroin is detected in the system. *See* McGuire_Public_Nuisance_Tables.xlsx, tab "Table 2."
[263] McGuire_Public_Nuisance_Tables.xlsx, tab "Table 2."
[264] Alison L. Pitt et al., "Modeling Health Benefits and Harms of Public Policy Responses to the US Opioid Epidemic," *American Journal of Public Health* 108, 2018, no. 10, pp. 1394–400 at p. 1395, Supplement pp. S4–S5.
[265] RAND Corporation, "What America's Users Spend on Illegal Drugs: 2000–2010," *Office of National Drug Control Policy Report*, February 2014, pp. 23–25.
[266] RAND Corporation, "What America's Users Spend on Illegal Drugs: 2000–2010," *Office of National Drug Control Policy Report*, February 2014, pp. 23–25.

of days an individual could have OUD in 2014. This assumption is surely an overestimate, and fails to account for individuals who acquire the condition mid-year or who enter recovery mid-year.

153. Professor McGuire's cost-benefit analysis is also unreliable because he assumes that OUD and pain affect quality of life equally. Despite noting that days with a health condition could be weighted based on the "relative importance" of the condition using QALYs, he asserts that the QALY impacts of shipments can be assessed by comparing days of OUD with days of pain relief because "the estimates from the literature on the QALY gain from pain treatment are in overlapping ranges as the QALY lost from living with OUD."[267] This is a gross oversimplification. Both OUD and pain are complex conditions, and as noted by Professor McGuire, there is considerable variation in the QALY estimates for each condition reported in the literature.[268] Published studies show that in the population with OUD, the impacts of OUD on QALY vary with comorbid conditions, use of treatment, and presence of polysubstance abuse, for example.[269] Analyses of the QALY impacts of pain show that the impact varies with the severity of pain.[270] To properly assess the QALY impacts of OUD versus pain relief, Professor McGuire would need to account for these characteristics and their representativeness of the populations purportedly affected by shipments in the Plaintiff Counties.

154. In sum, Professor McGuire has stacked the deck against a finding that the benefits of opioids outweigh the costs in terms of their impact on QALYs. He does so by excluding pain relief for chronic pain patients from his calculations, overstating the number of OUD days caused by shipments by double counting concurrent prescription OUD and heroin use disorder ("HUD"), and relying on Professor Cutler's inflated estimates of the relationship between shipments and opioid-related harms.

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[267] McGuire Public Nuisance Report, ¶¶ 83–84.
[268] McGuire Public Nuisance Report, ¶¶ 84–85, FN 115–118.
[269] Jessica De Maeyer et al., "Quality of Life among Opiate-Dependent Individuals: A Review of the Literature," *International Journal of Drug Policy* 21, no. 5, 2010, pp. 364–80 at p. 376.
[270] Sarah Wetherington et al., "Pain Quality of Life as Measured by Utilities," *Pain Medicine* 15, pp. 865–70 at p. 868 and Table 2. Wetherington et al. note that for the subjects in their study, "as pain severity increased, utility scores decreased."

Workforce Participation and Productivity

155. To reach his opinion that the costs of opioid shipments outweigh their benefits in terms of impacts on workforce participation and productivity, Professor McGuire reviews research on this topic. Some of the research Professor McGuire cites does not attempt to identify a causal relationship between opioid prescriptions and labor force participation and productivity and instead just notes correlations.[271] Three of the papers Professor McGuire cites, however, use an instrumental variables technique to attempt to identify causal impacts.[272] The findings from these three papers are mixed: two find negative effects of opioid prescribing on workforce participation (Savych et al. (2018) and Harris et al. (2019)), while one finds positive effects of opioid prescribing on female work force participation and no effect on male workforce participation (Currie et al. (2018)). The different findings may stem from differences in the populations studied, the validity of the instrumental variables used, or the variation used to identify a relationship between opioid prescribing and workforce participation and productivity. Of these three studies, only Currie et al. (2018) study the entire U.S. population, using county-level variation in opioid prescribing to identify the impact.[273] Of the other two papers, one focuses on a sample of workers with lower-back injuries in 28 states not including Ohio[274] and

[271] For example, Professor McGuire notes that one of the papers he cites "found that areas with higher opioid prescription rates have lower rates of labor force participation overall." *See* McGuire Public Nuisance Report, ¶ 75. The author of that paper, Professor Alan Krueger of Princeton University, noted that "it is unclear whether these correlations represent causal effects…." *See* Alan B. Krueger, "Where Have All the Workers Gone? An Inquiry into the Decline of the U.S. Labor Force Participation Rate," *Brookings Papers on Economic Activity Conference Drafts*, September 7–8, 2017, p. 4. Another paper McGuire cites also suffers from identification issues because it follows a similar approach to Krueger (2017), though it does attempt to rule out reverse causality after presenting the base specification. *See* Dionissi Aliprantis and Mark E. Schweitzer, "Opioids and the Labor Market," Federal Reserve Bank of Cleveland Working Paper No. 18-07, May 2018, pp. 2, 19, 23, 26.

[272] Bogdan Savych et al., "Do Opioids Help Injured Workers Recover and Get back to Work? The Impact of Opioid Prescriptions on Duration of Temporary Disability," NBER Working Paper No. 24528, April 2018, pp. i, 12; Matthew C. Harris et al., "Prescription Opioids and Labor Market Pains: The Effect of Schedule II Opioids on Labor Force Participation and Unemployment," *The Journal of Human Resources* 54, no. 2, January 2019, pp. 1, 18–19; Janet Currie et al., "U.S. Employment and Opioids, Is There a Connection?," NBER Working Paper No. 24440, March 2018, pp. 8, 20.

[273] Janet Currie et al., "U.S. Employment and Opioids: Is There a Connection?," NBER Working Paper No. 24440, March 2018.

[274] Bogdan Savych et al., "Do Opioids Help Injured Workers Recover and Get back to Work? The Impact of Opioid Prescriptions on Duration of Temporary Disability," NBER Working Paper No. 24528, April 2018, p. 6 and FN 9.

the other focuses on the population in ten states.[275] Based on these mixed findings, Professor McGuire states that "I am of the opinion that the short-term effect of shipments on work results in a negative relationship: more shipments means less work."[276] It is not clear how he reaches this opinion based on the mixed evidence he examines. It is my opinion that the research cited by Professor McGuire does not provide a clear answer on the impact of opioid prescribing on workforce participation or productivity.

156. Professor McGuire goes on to claim that Professor Cutler has shown "the harmful effects of prescriptions today continue for years" and, according to Professor McGuire, these "longer-term harmful effects likely apply to work-related disabilities as well."[277] As noted above, Professor Cutler has not performed a causal analysis, but has instead only demonstrated correlation between shipments and opioid mortality. It bears repeating that correlation is not causation. Moreover, as discussed in Section V, my review of Professor Cutler's analysis demonstrates that his estimated correlation is substantially reduced once I take into account, at least in part, underlying despair impacting both opioid use and mortality that Professor Cutler omits from his model. Finally, even if one believes there are long-term harmful effects from opioid shipments, Professor McGuire makes no attempt to assess potential long-term beneficial effects, such as being able to sustain steady employment and maintain engagement in activities of daily life,[278] the other side of any reasonable cost-benefit analysis.

157. In sum, Professor McGuire's opinion that opioid prescribing has negative impacts on QALYs and workforce productivity is not based on reliable evidence. As a result, he has not demonstrated that the interference from opioid shipments was unreasonable.

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[275] Matthew C. Harris et al., "Prescription Opioids and Labor Market Pains: The Effect of Schedule II Opioids on Labor Force Participation and Unemployment," *The Journal of Human Resources* 54, no. 2, January 2019, pp. 13–14. The ten states are Arkansas, California, Colorado, Florida, Massachusetts, Michigan, Ohio, Oregon, Tennessee, and Texas.

[276] McGuire Public Nuisance Report, ¶ 76.

[277] McGuire Public Nuisance Report, ¶ 77.

[278] Professor Cutler acknowledged there are a number of potential benefits from prescription opioids beyond pain relief. *See* Cutler Deposition, 153:23-154:1.

C. Professor McGuire's Opinion that Defendants Were Aware or Should Have Been Aware That Their Allegedly Misleading Statements Constituted an Interference

158. Professor McGuire opines that Defendants were aware or should have been aware that their allegedly misleading statements constituted an interference. He bases this opinion entirely on the opinions of other Plaintiffs' experts related to Defendants' marketing and his review of Defendants' settlements with government entities. Professor McGuire notes that, according to Drs. Perri, Kessler, and Egilman, manufacturer Defendants knew or should have known "they were making misleading statements about the safety and efficacy of the prescription opioids they manufactured."[279] Yet, as discussed in Section IV, since the early 2000s, Purdue has undertaken a number of efforts to make prescribers aware of the risks of opioid products and disseminate accurate information about these risks.[280] Professor McGuire ignores all of these efforts.

159. Professor McGuire also claims that Purdue's 2007 settlement with the U.S. Government shows that Purdue had "clear knowledge that the shipments had negative impacts on the public health and safety of communities across the nation, including in the Bellwether communities."[281] Specifically, he notes that "Purdue admitted that from December 12, 1995 to June 30, 2001, 'certain Purdue supervisors and employees, with the intent to defraud or mislead, marketed and promoted OxyContin as less addictive, less subject to abuse and diversion, and less likely to cause tolerance and withdrawal than other pain medications…'" and that "Purdue acknowledged that it 'manufactured, marketed, and sold quantities of OxyContin in interstate commerce from various locations….'"[282] It is not clear how these statements *per se* support an opinion that Purdue knew or should have known that its shipments (both those impacted and those not impacted by its marketing) were significantly interfering with public health, safety, peace, and comfort. None of these statements admit to any such interference. Moreover, the addition of a black box warning related to addiction and overdose risk to the OxyContin label in 2001 and all of Purdue's subsequent efforts related to warning of the risk of opioid addiction and abuse would

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[279] McGuire Public Nuisance Report, ¶ 90.
[280] "OxyContin Abuse and Diversion and Efforts to Address the Problem," United States General Accounting Office Report to Congressional Requesters, No. GAO-04-110, December 2003.
[281] McGuire Public Nuisance Report, ¶¶ 91–92.
[282] McGuire Public Nuisance Report, ¶ 92.

have given Purdue reason to believe that any interference caused by early problematic marketing messages would have dissipated quickly.[283]

160. If instead Professor McGuire is suggesting that because it was known that prescription opioids carry an addiction and overdose risk, Defendants, including Purdue, should have known that sales of their products constituted an unreasonable interference, this opinion is again inconsistent with the actions of the FDA. As noted above, the FDA continues to allow these products to be sold and marketed for uses that Professor McGuire assumes are clinically unjustified.[284] Similarly, as mentioned above, a number of federal and state agencies (such as CMS and State Medicaid agencies) continue to reimburse for such uses of prescription opioids and even the Plaintiffs have continued to do so through 2018.[285] This indicates that these entities have not concluded the costs of opioid treatment outweigh the benefits or that prescription opioid shipments cause an unreasonable interference.

D. Professor McGuire's Public Nuisance Cost Estimates

161. As discussed above, Professor McGuire's estimates for the opioid-related harms allegedly caused by prescription opioid shipments are deeply flawed. His monetary valuation of these harms is also flawed, as outlined below.

1. Mortality: Deaths

162. Professor McGuire uses the value of a statistical life ("VSL") to quantify the cost of each death attributable to shipments.[286] Specifically, Professor McGuire utilizes a cost of $9.3 million (2014) for each death purportedly due to shipments, following U.S. Department of Health and Human Services (HHS) 2016 guidelines based on estimates provided by Robinson and Hammitt

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[283] OxyContin Abuse and Diversion and Efforts to Address the Problem," United States General Accounting Office Report to Congressional Requesters, No. GAO-04-110, December 2003, p. 34.
[284] FDA OxyContin Label, April 2014, PPLP003275296–307 at 296; Letter from FDA to Physicians for Responsible Opioid Prescribing, "Re: Docket No. FDA-2012-P-0818," September 10, 2013, p. 1.
[285] CMS, Data Analysis Brief: National Trends in High-Dose Chronic Opioid Utilization among Dual Eligible and Medicare-Only Beneficiaries (2006–2015), October 2018; Cuyahoga and Summit County medical and pharmacy claims data.
[286] McGuire Public Nuisance Report, Table 4.

(2016).[287] This value is derived from a review of various papers that utilize either survey methods or wage-risk methods to estimate VSL. In survey methods, individuals are asked about their willingness-to-pay for a small reduction in the probability of their own death.[288] In wage-risk methods, VSL is inferred from wage differences between jobs that entail different levels of fatality risk.[289] For his estimates for Cuyahoga and Summit Counties, Professor McGuire adjusts the 2014 $9.3 million cost per death to account for inflation and the county's median income in the year of interest.[290]

163. VSL is not a reliable measure of harm from fatalities as can be seen from how widely estimates of VSL vary. For example, Robinson and Hammitt (2016) cite estimates of VSL for U.S. workers as low as $2.1 million and as high as $20.8 million in 2013 dollars—that is, the high end is ten times the low end.[291] Economists have also questioned the validity of survey-based VSL estimates, because they are hypothetical in nature. For example, in their review of the literature, Cropper, Hammitt, and Robinson (2011) note "individuals may give spurious answers because they face no real consequences."[292] Estimates of VSL based on wage premiums associated with riskier jobs have also been critiqued in the literature as biased because they are "plagued by measurement error and omitted variables."[293] In the Lee and Taylor (2014) paper reviewed by Robinson and Hammitt (2016), the authors estimated much lower VSLs than the VSL used by Professor McGuire ($2.1 to $4.1 million in 2013 dollars) when they attempted to correct for these issues.[294]

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[287] McGuire Public Nuisance Report, ¶ 113; Lisa A. Robinson and James K. Hammitt, "Valuing Reductions in Fatal Illness Risks: Implications of Recent Research," *Health Economics* 25, 2016, pp. 1039–52 at p. 1045.
[288] McGuire Public Nuisance Report, Appendix C, p. C-1; Lisa A. Robinson and James K. Hammitt, "Valuing Reductions in Fatal Illness Risks: Implications of Recent Research," *Health Economics* 25, 2016, pp. 1039–52.
[289] McGuire Public Nuisance Report, Appendix C, p. C-1.
[290] McGuire Public Nuisance Report, Appendix C, p. C-2.
[291] Lisa A. Robinson and James K. Hammitt, "Valuing Reductions in Fatal Illness Risks: Implications of Recent Research," *Health Economics* 25, 2016, pp. 1039–52 at p. 1044; Maureen L. Cropper et al., "Valuing Mortality Risk Reductions: Progress and Challenges," NBER Working Paper No. 16971, pp. 12, 22; W. Kip Viscusi, "The Flawed Hedonic Damages Measure of Compensation for Wrongful Death and Personal Injury," *Journal of Forensic Economics* 20, no. 2, April 2011, pp. 113–35 at p. 116.
[292] Maureen L. Cropper et al., "Valuing Mortality Risk Reductions: Progress and Challenges," NBER Working Paper No. 16971, April 2011, p. 14.
[293] Jonathan M. Lee and Laura O'Taylor, "Randomized Safety Inspections and Risk Exposure on the Job: Quasi-Experimental Estimates of the Value of a Statistical Life," Center for Economic Studies Working Paper No. 14-05, January 2014 ("Lee and Taylor (2014)"), p. i.
[294] Lee and Taylor (2014), pp. i, 31.

164. Further, VSL has not been widely used to measure the cost of fatalities in litigation, nor has it been commonly accepted in academic research settings. For example, settlements from the tobacco and asbestos litigations did not include costs of fatalities based on VSL.[295] Indeed, Professor McGuire noted in deposition that prior to this litigation, he had never used VSL to quantify costs in a lawsuit.[296] Among the six academic research and policy reports cited by Professor McGuire as providing estimates of the economic burden of the opioid crisis, only one—the CEA report—uses VSL to measure the cost of fatalities.[297] The two community assessments of the opioid crisis referenced by Professor McGuire do not use VSL.[298] Instead, these studies have estimated the cost of fatalities based on earnings and productivity losses, which provide much smaller costs per death than VSL. Professor McGuire's costs of mortality are dramatically inflated relative to these studies. For example, Professor McGuire's VSL methods would estimate the cost of all U.S. opioid-related deaths in 2013 to be over $148 billion, whereas research cited by Professor McGuire indicates that cost to be less than one-sixth the size—$22 billion.[299]

165. Professor McGuire's adjustment of VSL also fails to capture values specific to the population of Cuyahoga and Summit County individuals who had opioid-related deaths. Studies have shown that VSL varies based on characteristics including age, the type of illness preceding death, and risk preferences, among others.[300] In particular, prior research has indicated that

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[295] Third Amendment to and Complete Restatement of Western Asbestos Settlement Trust Case Valuation Matrix, undated; W. Kip Viscusi and Joni Hersch, "Tobacco Regulation through Litigation: The Master Settlement Agreement" in *Regulation v. Litigation: Perspectives from Economics and Law*, ed. Daniel P. Kessler (Chicago: University of Chicago Press, 2010).

[296] McGuire April 30 Deposition, 703:25–704:2.

[297] The Underestimated Cost of the Opioid Crisis," The Council of Economic Advisors Executive Summary, November 2017, p. 3.

[298] Altarum, "Community Assessment of the Opioid Crisis in Lorain County, Ohio," Nord Family Foundation Executive Summary, December 20, 2017, p. 1; Mark Rembert et al., "Taking Measure of Ohio's Opioid Crisis," C. William Swank Program in Rural-Urban Policy Report, October 2017.

[299] Curtis S. Florence et al., "The Economic Burden of Prescription Opioid Overdose, Abuse, and Dependence in the United States, 2013," Medical Care 54, no. 10, 2016, pp. 901–6 at p. 904.

[300] James K. Hammitt and Kevin Haninger, "Valuing Fatal Risks to Children and Adults: Effects of Disease, Latency, and Risk Aversion," *Journal of Risk and Uncertainty* 40, 2010, pp. 57–83 at pp. 60–61; Trudy Ann Cameron and J.R. DeShazo, "Demand for Health Risk Reductions," *Journal of Environmental Economics and Management* 65, 2013, pp. 87–109; W. Kip Viscusi, "The Flawed Hedonic Damages Measure of Compensation for Wrongful Death and Personal Injury," *Journal of Forensic Economics* 20, no. 2, 2007, pp. 113–35; W. Kip Viscusi, "Policy Challenges of the Heterogeneity of the Value of Statistical Life," *Foundations and Trends in Microeconomics* 6, no. 2, 2010, pp. 99–172 at pp. 108–9.

"[p]eople who choose…very risky products… have revealed themselves to have lower VSL levels than the average person in society."[301] To the extent that drug users or those who would misuse opioids are less risk-averse than the general population on average,[302] Professor McGuire has overestimated VSL.

2. Morbidity: OUD Cases

166. I have described problems with Professor McGuire's inflation of NSDUH numbers of OUD in Section VII.B. Excluding Professor McGuire's inflation of the NSDUH data reduces his estimate of overall nuisance costs (2006–2016) due to OUD by 35 percent in each County.[303] In addition to this concern, the OUD measure in the NSDUH survey is based on all "Pain Reliever Abuse or Dependence."[304] The NSDUH survey includes Fioricet and Fiorinal (both barbiturates) in this measure, indicating that some cases of OUD estimated by Professor McGuire may not be opioid related at all.[305]

3. Babies with NAS

167. Professor McGuire adopts counts of NAS births from Summit and Cuyahoga Counties without limiting these counts to instances of NAS resulting from abuse of opioids as opposed to

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[301] W. Kip Viscusi, "Policy Challenges of the Heterogeneity of the Value of Statistical Life," *Foundations and Trends in Microeconomics* 6, no. 2, 2010, pp. 99–172 at p. 110.
[302] Serge Blondel et al., "Rationality and Drug Use: An Experimental Approach," *Journal of Health Economics* 26, 2007, pp. 643–58.
[303] This result is obtained by setting the OUD rate in tab "Table 2" of McGuire_Public_Nuisance_Tables.xlsx equal to the NSDUH HUD Rate plus the NSDUH Pain Reliever Use Disorder Rate.
[304] National Survey on Drug Use and Health, 2000–2017.
[305] National Survey on Drug Use and Health, 2000–2017. Notably, NSDUH survey estimates also appear to dramatically overestimate the number of individuals who use OxyContin. For example, IQVIA data indicate that 0.8 million patients received OxyContin prescriptions in 2015, while NSDUH estimates that 7.5 million individuals used OxyContin (not including those who misused OxyContin) that same year. Because those using, but not misusing, should have a prescription, this suggests that NSDUH is overstating the number of OxyContin users by a factor of almost ten. The discrepancy has only increased since then. In 2017, IQVIA data indicate that 0.5 million patients received OxyContin prescriptions, while in the same year, NSDUH data estimate that 7.5 million individuals used OxyContin (again, not including those who misused OxyContin). Individuals may be equating oxycodone or opioids more generally with OxyContin and thus over-reporting OxyContin use.

abuse of other addictive substances.[306] As a result, Professor McGuire overstates the number of opioid-related NAS births purportedly due to shipments.

168. Professor McGuire's estimates of the cost per baby with NAS is based on the difference in average costs between babies born with NAS and all babies born in a given year, using data provided by the Ohio Department of Health.[307] This method assumes that but for opioid shipments, babies born with NAS would have had costs similar to the average baby in the Counties, yet such an assumption is unlikely to be true. Consider a mother who has a child born with NAS because she took opioids during pregnancy due to a medical condition. In such cases, the underlying medical condition itself might have led to an increased cost of birth had the mother not been exposed to opioids. Alternatively, for pregnant women with OUD, Professor McGuire has not assessed the likelihood of non-opioid substance abuse that might have also led to high costs of birth. This oversight is particularly problematic given the extent of polysubstance abuse among individuals with OUD.[308] By failing to take into account factors that are correlated with both opioid use during pregnancy and high costs of birth, Professor McGuire has overestimated the cost of birth for a baby born with NAS.

4. Crimes

169. Professor McGuire estimates the total cost of crime due to shipments, including crimes reported by all law enforcement divisions for which Plaintiff County data are available.[309] To estimate the number of crimes due to shipments, he first obtains counts of total crimes in each county by crime type (*e.g.*, arson, burglary, murder) from the National Incident-Based Reporting System. He multiplies total crimes in each county by the share of crimes that are opioid related, based on Professor Cutler's methodology, and then by Professor Cutler's estimates of the share

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[306] McGuire Public Nuisance Report, Appendix E, pp. E-1–3. NAS is not limited to opioid-related cases. As defined by SAMHSA, NAS refers to signs of withdrawal in "[f]etuses exposed to tobacco, alcohol, prescription medications (*e.g.*, benzodiazepines), and illicit substances." *See* Substance Abuse and Mental Health Services Administration, "Clinical Guidance for Treating Pregnant and Parenting Women with Opioid Use Disorder and Their Infants," Department of Health and Human Services Publication No. (SMA) 18-5054, 2018, p. 4.

[307] McGuire Public Nuisance Report, Appendix E, pp. E3–5.

[308] According to NSDUH data, between 2006 and 2014, an average of 42 percent of individuals with OUD nationally also had another SUD at the same time.

[309] Professor McGuire's crime counts by crime category are from the National Incident-Based Reporting System (NIBRS) data for Cuyahoga and Summit counties. *See* McGuire Public Nuisance Report, Appendix F, pp. F-1–2.

of opioid-related harms that are purportedly due to shipments. Finally, Professor McGuire multiplies his estimate of opioid-related crimes due to shipments by the cost per crime for each crime type to obtain total costs of crime due to shipments in the Plaintiff Counties.[310]

170. Professor McGuire applies a cost per crime based on crime type, and within three categories of cost: direct costs to the crime victim (*e.g.*, property loss, medical expenses, expenditures on crime deterrents), implicit costs (productivity losses of victims and perpetrators), and intangible costs (pain and suffering and the adjusted risk-of-homicide). The cost per crime by crime type is adopted from McCollister et al. (2010) when available and from Miller and Bhattacharya (2013) otherwise.[311]

171. Professor McGuire makes several errors that inflate his costs. A basic conceptual error is that Professor McGuire does not properly identify incremental costs relative to the counterfactual scenario in which the crime had not occurred. McCollister et al. (2010) note "[A] limitation with the crime cost estimates presented here is that they reflect the average cost per crime as opposed to the more policy relevant marginal cost." The authors further note that the average cost per crime "could potentially overstate the marginal value of each additional criminal act avoided."[312]

172. For example, consider a program serving 100 people that costs $100,000 to set up and then $1,000 for each person served. The total cost of this program is $200,000 (the sum of the set-up cost and the total operational cost), the average cost per person is $2,000 (the total cost divided by the number of people), and the incremental cost per person is $1,000 (excluding the set-up cost). Unless the entire program would not have been needed and would never have been set up absent shipments, damages should be based on the incremental cost of $1,000 per person, not the average cost per person of $2,000. This difference between incremental or marginal costs and average costs is a basic concept taught in introductory economics classes and yet one that Professor McGuire ignores in his public nuisance cost estimates.

173. Professor McGuire also makes several errors when identifying the types of costs that should be included in his estimation of the nuisance. For example, when using costs per crime

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[310] McGuire Public Nuisance Report, Appendix F, pp. F-1–2.
[311] McGuire Public Nuisance Report, Appendix F, pp. F-8–9.
[312] Kathryn E. McCollister et al., "The Cost of Crime to Society: New Crime-Specific Estimates for Policy and Program Evaluation," *Drug and Alcohol Dependence* 108, nos. 1–2, 2010, pp. 1–26 ("McCollister et al. (2010)") at p. 16.

from Miller and Bhattacharya (2013), Professor McGuire includes costs for "public services," which are duplicative of his costs to the Plaintiffs.[313] If I remove the cost of public services from the cost per crime values Professor McGuire adopts from Miller and Bhattacharya, his estimate of crime costs due to shipments decreases by over 15 percent in Cuyahoga County and over 29 percent in Summit County.[314]

174. Finally, Professor McGuire provides no justification for his preference for cost values from McCollister et al. (2010) over Miller and Bhattacharya (2013) when both provide estimates for similar if not identical crime categories. If he had instead preferred Miller and Bhattacharya (2013)[315] and corrected the cost per crime to exclude "public services," his total cost of crime due to shipments would decrease by over 25 percent in Cuyahoga County and over 34 percent in Summit County.[316]

5. Child Maltreatment

175. Professor McGuire estimates the number of children maltreated as a result of opioid shipments by multiplying the number of maltreated children in the Plaintiff Counties by

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[313] If shipments of opioids led to costs to these public services, Professor McGuire should have identified them as relevant in his estimation of costs to the Plaintiffs. Indeed, Miller and Bhattacharya (2013) indicate that "police" are included in this category, which directly overlaps with Professor McGuire's costs to the sheriff's office in his estimation of costs to the Plaintiffs. *See* Ted Miller and Soma Bhattacharya, "Incidence and Cost of Carbon Monoxide Poisoning for All Ages, Pool and Spa Submersions for Ages 0–14, and Lead Poisoning for Ages 0–4," PIRE Final Report, Task Order 1, CPSC Contract No. D-09-0003, March 28, 2013, p. 39.

[314] These percentages use Professor McGuire's "Approach 1" figures.

[315] Notably, McCollister et al. (2010) cites prior work by Miller extensively, noting some publications authored by Miller were "instrumental in developing and refining crime-costing Methods." *See* McCollister et al. (2010), p. 3. Indeed, McCollister et al. (2010) repeatedly refers to work by Miller to motivate techniques used in their own paper. In addition to Miller and Bhattacharya (2013), Miller has produced a number of government reports and published articles on the cost of crime. *See*, *e.g.*, Ted Miller and Soma Bhattacharya, "Incidence and Cost of Carbon Monoxide Poisoning for All Ages, Pool and Spa Submersions for Ages 0–14, and Lead Poisoning for Ages 0–4," PIRE Final Report, Task Order 1, CPSC Contract No. D-09-0003, March 28, 2013; Ted R. Miller et al., "Costs of Alcohol and Drug-Involved Crime," Prevention Science 7, 2006, pp. 333–42; Ted R. Miller et al., "Victim Costs and Consequences: A New Look," National Institute of Justice Research Report No. 155282, January 1996, p. 1; Ted R. Miller et al., "Victim Costs of Violent Crime and Resulting Injuries," *Health Affairs*, 1993, pp. 186–97.

[316] For this calculation, I have also excluded costs associated with "adjudication and sanctioning" from Miller and Bhattacharya (2013), as consistent with Professor McGuire. If instead "public services" are included in the cost per crime, use of Miller and Bhattacharya (2013) when available leads to a reduction of over 5 percent in Cuyahoga County and over 1 percent in Summit County. These percentages use Professor McGuire's "Approach 1" figures. *See* Ted Miller and Soma Bhattacharya, "Incidence and Cost of Carbon Monoxide Poisoning for All Ages, Pool and Spa Submersions for Ages 0–14, and Lead Poisoning for Ages 0–4," PIRE Final Report, Task Order 1, CPSC Contract No. D-09-0003, March 28, 2013.

Professor Cutler's share of harms to the Division of Child and Family Services (Cuyahoga County) and to the Children Services Board (Summit County).[317] To estimate the total nuisance cost related to child maltreatment, Professor McGuire then applies an estimate of the cost per maltreated child due to lost earnings and special education needs, based on his review of the literature.[318]

176. Professor Cutler's estimate of the share of child services harms due to shipments is based on multiplying the share of opioid mortality that is due to shipments by the share of child removals that are opioid related.[319] Neither Professor Cutler nor Professor McGuire has assessed the share of overall child maltreatment that is opioid related. Child removals and child maltreatment are not the same thing, as demonstrated by Dr. Nancy Young, Executive Director of Children and Family Services, and a Plaintiffs' expert on whom Professor McGuire relies for an estimate of the number of children subject to maltreatment.[320] Notably, the number of children maltreated, as reported by Dr. Young, is substantially larger than the number of child removal entries also reported by Dr. Young.[321] For the years 2006 to 2016 in the Plaintiff Counties, she estimates 32,226 total children maltreated (23,090 in Cuyahoga County and 9,136 in Summit County) and 20,417 total children entering "out of home" (foster) care (11,148 in Cuyahoga County and 9,269 in Summit County).[322] Thus, Professor McGuire lacks a basis to evaluate the public nuisance costs for child maltreatment generally.

177. Professor McGuire uses lost earnings per child due to maltreatment from Currie and Widom (2010) and special education costs based on combining parameters from several papers.[323] The drivers of outcomes like special education needs and earnings are many and complex, and the estimates in these papers are not appropriate for the current conditions in the

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[317] In the case of child maltreatment, Professor McGuire applies Professor Cutler's share of harms to the Division of Child and Family Services (Cuyahoga County) and to the Children Services Board (Summit County), because Professor McGuire's counts of maltreated children are not isolated to cases that are opioid-related. *See* McGuire Public Nuisance Report, Appendix G.
[318] McGuire Public Nuisance Report, ¶ 130.
[319] Cutler Report, ¶ 44, Table I.6.
[320] McGuire Public Nuisance Report, ¶ 58.
[321] Expert Report of Nancy K. Young, Ph.D., March 25, 2019 ("Young Report"), Graphic 12, Graphic 13, and Graphic 15.
[322] Young Report, Graphic 12, Graphic 13, and Graphic 15.
[323] McGuire Public Nuisance Report, Appendix G, Appendix G, pp. G-3–4.

Plaintiff Counties. For example, Currie and Widom (2010) analyze the earnings of adults from 2003 to 2004 based on exposure to abuse or neglect in the 1960s and 1970s, yet Professor McGuire is assessing instances of maltreatment from 2006 to 2016.[324] Given changes in access to social services and child welfare practices over time,[325] Professor McGuire has no basis to believe that the quantitative impact of abuse on productivity will be the same for children exposed to maltreatment today as it was for children exposed nearly half a century ago. In addition, none of the studies used by Professor McGuire focus on current conditions in Ohio, and Professor McGuire has not assessed the validity of his estimates to conditions in the Plaintiff Counties in particular.

6. Costs to Plaintiffs

178. Having calculated public nuisance costs resulting from the five types of harms enumerated above, Professor McGuire then adds to them his damages estimate from his Damages Report, but scaled up to reflect the purported impact of all prescription opioid shipments, not just the portion of shipments attributed to Defendants' alleged misconduct. Professor McGuire opines that the resulting sum comprises the total public nuisance purportedly imposed by shipments of prescription opioids.[326] In Section VI, I have described the flaws in Professor McGuire's estimation of damages and these flaws apply equally to his public nuisance estimate of cost to Plaintiffs. Notably, Professor McGuire's total public nuisance estimate includes the same costs as his damages estimate. As such, it would be inappropriate to add the two together.

179. In summary, Professor McGuire's opinions regarding the public nuisance purportedly caused by prescription opioid shipments to the Plaintiff Counties are based on a series of unfounded assumptions, biased parameter estimates, and execution errors. As a result, he has failed to demonstrate that shipments of prescription opioids led to any public nuisance in the Plaintiff Counties, let alone provided any reliable cost estimates of the purported nuisance.

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[324] Janet Currie and C.S. Widom, "Long-Tern Consequences of Child Abuse and Neglect on Adult Economic Well-Being," *Child Maltreatment* 15, no. 2, 2010, pp. 111–120 at p. 1.
[325] *See* discussion in "Concept and History of Permanency in U.S. Child Welfare," Child Welfare Information Gateway, 2016, https://www.childwelfare.gov/topics/permanency/overview/history/.
[326] McGuire Public Nuisance Report, ¶ 135.

VIII. Review of Plaintiffs' Experts' Abatement Cost Analyses and Opinions

180. Professor Liebman and Dr. Alexander each provide estimates of the costs required to abate the opioid crisis based on forecasts over 10 or 15 years into the future. The validity of such predictions has been a prominent concern among economists since at least 1976, when Nobel laureate Robert Lucas articulated a fundamental problem with forecasting the impact of policy changes: predictions of policy outcomes based on historical data often assume that the relationships between variables as measured in the data will persist after a change in policy, when in fact the policy change itself may fundamentally alter the economic environment such that these relationships no longer hold.[327] It is for this reason that Lucas wrote, "simulations using [econometric] models can, in principle, provide no useful information as to the actual consequences of alternative economic policies."[328]

181. The forecasts of Professor Liebman and Dr. Alexander are subject to this problem. Both seek to predict future abatement costs that are based on complex relationships between choices made by individuals to use or to prescribe opioids, and their consequences, such as the prevalence of OUD, and the implications for the costs of social services and criminal justice programs. Critically, their forecasts of these outcomes are based on measurements from historical data, which are the direct result of the policies in place at the time of the measurement. There is no reason to believe that these relationships will operate in the same way in a different environment, where the introduction of a new abatement policy or program may alter the behavior of individuals or physicians in a way that has not been captured by historical data. This is why economists prefer to develop predictions founded on explicit models of how individuals respond to their economic environment, rather than on empirical regularities observed in historical data.

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[327] As Lucas himself put it, "[G]iven that the structure of an econometric model consists of optimal decision rules of economic agents, and that optimal decision rules vary systematically with changes in the structure of series relevant to the decision maker, it follows that any change in policy will systematically alter the structure of econometric models." Lucas, Robert E. "Econometric policy evaluation: A critique," in *Carnegie-Rochester conference series on public policy*, vol. 1, no. 1, 1976, pp. 19–46 at p. 41 ("Lucas (1976)"). In particular, awareness of policy changes may alter the decision-making of individuals, which may in turn change the relationship between inputs to an economic model and its outcomes.

[328] Lucas (1976) (emphasis in original). Though the "Lucas critique" was first raised in the context of macroeconomic and monetary policy, it applies very broadly to forecasting models.

182. Neither Professor Liebman nor Dr. Alexander appear to recognize this problem, and neither of them base their predictions on the type of analysis which establishes the "policy-invariant parameters" that are the foundations of a reliable forecasting model. Further, neither Professor Liebman nor Dr. Alexander have taken the basic step of testing how robust predictions are to changes in their assumptions and modeling choices, or to "noise" or errors in the data.

A. Review of Professor Liebman's Analysis and Opinions

183. Professor Liebman presents a 15-year plan consisting of 19 programs and associated cost estimates that would purportedly abate the opioid crisis in the Plaintiff Counties.[329] As discussed in greater detail below, this analysis is fundamentally flawed because Professor Liebman fails to identify and isolate the incremental abatement costs required due to any alleged misconduct by Defendants. Beyond this, Professor Liebman's analysis is generally unreliable because it crucially depends on unsupported assumptions about how treatment needs in the Plaintiff Counties will evolve from 2020 to 2034, including assumptions that are contradicted by current trends and the opinions of other Plaintiffs' experts.

1. Types of Abatement Costs Included in Professor Liebman's Analysis

184. To begin with, Professor Liebman readily admits he offers no opinion regarding the role or responsibilities of any Defendant in causing the opioid crisis.[330] He also includes in his analysis costs for treating individuals for addiction and substance abuse even though some of these individuals never used any prescription opioids, let alone any of Defendants' products.

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[329] The Liebman Initial Report included costs for seven out of the 19 programs included in Professor Liebman's abatement plan. A week later, Professor Liebman submitted his Supplemental Report which provided costs for the remaining 12 programs, while also updating the costs for the two of the seven programs included in the Liebman Initial Report. Approximately two weeks after submitting his Supplemental Report, Professor Liebman submitted a "corrected" version of his Appendix D that contained updated costs for one of the programs included in the Liebman Supplemental Report. For the remainder of this section, I refer to the Liebman Supplemental Report and the corrected Appendix D for Professor Liebman's final cost estimates and methods. Further, in his deposition, Professor Liebman testified that he had updated the cost for yet another program—social support housing—but he has yet to produce an updated appendix with this correction. Deposition of Jeffrey Liebman, May 3, 2019 ("Liebman Deposition"), 72:22–76:2.

[330] Liebman Deposition, 63:15–64:24.

Professor Liebman himself acknowledges this,[331] but makes no attempt to correct for this flaw in his calculations. This flaw affects Professor Liebman's two largest programs—medication-assisted treatment ("MAT") and treatment excluding MAT—which jointly account for over two thirds of Professor Liebman's total abatement cost estimates and amount to $3.1–$4.1 billion in Cuyahoga County and $1.4–$1.8 billion in Summit County.[332]

185. Specifically, Professor Liebman estimates the number of individuals who will require treatment for addiction and substance-related disorders based on the same combined 2016 prescription OUD and HUD prevalence that Professor McGuire uses for his public nuisance estimates.[333] As a result, his estimates suffer from the same flaw as Professor McGuire's, *i.e.*, double counting individuals who concurrently abuse prescription opioids and use heroin. (*See* Section VII.) Professor Liebman's estimates, however, suffer from an additional flaw. Unlike Professor McGuire who at least attempts (albeit unsuccessfully) to limit his estimates to the share of the population whose prescription OUD or HUD can be purportedly linked to prescription opioid shipments, Professor Liebman calculates abatement costs for the entire population with prescription OUD or HUD. As a result, Professor Liebman includes in his cost estimates individuals whose substance abuse disorder has been shown by Plaintiffs' own experts to be unrelated to any conduct by Defendants.

186. The same flaw impacts not only his addiction and substance abuse treatment costs, but also a number of Professor Liebman's estimates of costs associated with providing a range of other services to individuals whose substance abuse disorder cannot be linked to any conduct by Defendants. This affects another five of Professor Liebman's programs, for which he estimates costs amounting to $544.9–$545.8 million for Cuyahoga County and $170.4–$171.0 million for Summit County.[334] These programs include home visits for pregnant women with OUD, treatment and transitional housing for inmates with OUD, syringe exchange program participants with OUD, human immunodeficiency virus ("HIV") and hepatitis C virus ("HCV") treatment costs for individuals with opioid-related HIV/HCV and transitional housing for homeless

[331] Liebman Supplemental Report, FN 7.
[332] Liebman Supplemental Report, Tables 1–2.
[333] Liebman Supplemental Report, corrected Appendix D; McGuire Public_Nuisance_Tables.xlsx.
[334] Liebman Supplemental Report, corrected Appendix D.

individuals with OUD. Consider Professor Liebman's estimate for the share of individuals with "opioid-related" HIV/HCV, which appears to be entirely based on statistics regarding heroin users.[335] Professor Liebman makes no attempt to determine what share, if any, of the heroin use of individuals diagnosed with HIV or HCV can be in any way linked to conduct by Defendants. This is particularly relevant given that a number of heroin users never used prescription opioids, as acknowledged by Professor Liebman.[336] Similarly, Professor Liebman's estimate for the number of opioid-related NAS cases, the initial input for his cost estimates for the home visit program, is taken directly from Professor McGuire's report. As a result, it suffers from the same flaw I noted in Section VII, namely the unsupported assumption that any NAS case in the Plaintiff Counties was caused by opioid use rather than use of other drugs also known to cause NAS.

187. This flaw also affects a number of other "opioid-related" costs included in Professor Liebman's abatement plan for which no relation to Defendants' alleged misconduct has been established. This flaw affects his third largest program—child welfare services—accounting for $303.6 million in Cuyahoga County and $227.4 million in Summit County, as well as five other of Professor Liebman's programs, for a total of $564.3–$582.8 million in Cuyahoga County and $331.8–$340.0 million in Summit County.[337] For example, Professor Liebman includes costs for providing child welfare services to children who purportedly were removed from their homes for "opioid-related" reasons. His estimate for the share of removals that were "opioid-related" is directly taken from Professor Cutler's report.[338] However, Professor Cutler's estimate includes all children taken into state custody whose parents were using opioids at the time of removal and is not in any way limited to cases where parental exposure to opioids was the cause for the children's removal from their homes.[339] For example, this calculation does not account for the fact that children whose parents use opioids may be removed for reasons unrelated to their parents' opioid use. A parent could be responsibly taking prescription opioids for a legitimate medical need and still be deemed unfit to take care of her child. Moreover, even if abuse of

[335] Liebman Supplemental Report, corrected Appendix D.
[336] Liebman Supplemental Report, FN 7.
[337] In addition to child welfare services, the five other "opioid-related" programs are the programs dedicated to recruiting physicians to provide MAT, connecting individuals to services, providing naloxone kits to first responders, hiring additional law enforcement, and tracking the progress of abatement efforts.
[338] Liebman Supplemental Report, corrected Appendix D.
[339] Cutler Report, ¶ 44.

opioids did factor into the removal of the child from the home, in the absence of opioids, the parent may have abused a different substance that also would have resulted in the child being removed from the home. Further, there is no evidence that the OUD the parents suffered was because of any conduct by Defendants.

188. Similarly, the programs dedicated to recruiting physicians to provide MAT, connecting individuals to services, providing naloxone kits to first responders, hiring additional law enforcement, and tracking the abatement progress of the opioid crisis may all be "opioid-related" programs, but Professor Liebman fails to provide any evidence that the costs of these programs are incremental costs required due to any alleged misconduct by Defendants. For example, Professor Liebman's cost estimates for tracking the abatement progress in both Cuyahoga and Summit Counties appear to be based on "2018 personnel cost commitments for heroin/fentanyl crisis as reported by the Cuyahoga Medical Examiner's Office."[340] Yet, Gary Guenther, the Chief Investigator for the Summit County Medical Examiner's Office, testified that the increase in heroin and fentanyl deaths that his office observed was due to an increase in the supply of heroin and fentanyl from China and Mexico.[341] Professor Liebman makes no attempt to disentangle how much, if any, of the total resources devoted to the heroin/fentanyl crisis are incremental costs that would only be required due to Defendants' alleged misconduct rather than costs that Plaintiffs would have to bear regardless of Defendants' conduct, as part of regular monitoring of the entry of illicit drugs into their communities.

189. Furthermore, Professor Liebman includes costs for other programs that even he does not claim are "opioid-related" yet appear to be costs that Plaintiffs intend to hold Defendants responsible for. He includes programs that are focused on prevention rather than abatement. Prevention programs are not needed because of the opioid crisis, but instead, to the extent they are effective, should be in place regardless of whether a community is experiencing a drug-related crisis. For example, Professor Liebman's abatement plan includes $264 million for Cuyahoga County and $114 million for Summit County for school-based prevention programs. These programs include the implementation of a substance abuse prevention curriculum to be "delivered to every student from sixth grade through twelfth grade" in the two Counties, as well

[340] Liebman Supplemental Report, corrected Appendix D.
[341] Guenther Deposition, 60:16–61:10, 77:8–78:9.

as "resources so that every high school and middle school in [the two Counties] has a sufficient number of social workers to coordinate the school's efforts to connect at risk youth to services."[342] While such programs may be worthwhile, they cover very broad categories of substance abuse such as alcohol, tobacco, marijuana, and other illicit drugs, and are not just limited to prescription drug abuse, let alone prescription opioid abuse. In fact, a number of the programs contemplated by Professor Liebman also address topics such as violence and self-esteem.[343] Professor Liebman offers no explanation as to why Defendants should pay for programs that are not even related to opioid abuse in general, let alone programs entirely unrelated to Defendants' conduct.

190. Similarly, Professor Liebman includes costs for funding "medical provider education and outreach" aimed at "address[ing] overprescribing" and "spread[ing] best prescribing practices."[344] Not only is this type of program not strictly "opioid-related," but it also should have been in place long ago if Plaintiffs were concerned about negative outcomes from prescription drug abuse or overprescribing more generally. Indeed, as discussed in Section IV, data from the National Ambulatory Medical Care Survey show that the total number of medications dispensed or prescribed during physician office visits in the U.S. has increased steadily since at least 1996.[345] Purdue itself, as also discussed in Section IV, has supported physician education programs regarding proper opioid prescribing since at least 2001.

191. Lastly, Professor Liebman has not demonstrated that even if any of his proposed abatement programs were funded, Plaintiffs would spend the money effectively. This is a valid concern given that, as discussed above, Cuyahoga County has been mired in corruption scandals.

192. In sum, Professor Liebman purports to "utilize standard and widely accepted tools of empirical economic analysis."[346] Yet, his abatement plan includes costs necessary to abate not only the opioid crisis in the Plaintiff Counties, but in some cases consequences of abuse of other substances, as well as even broader problems such as general overprescribing by medical providers. As a result, it contradicts basic economic principles about the meaning of incremental

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[342] Liebman Supplemental Report, ¶ 76.
[343] *See*, *e.g.*, "LST Overview," Botvin LifeSkills Training, https://www.lifeskillstraining.com/lst-overview/, accessed May 1, 2019; "Start Taking Alcohol Risks Seriously (STARS) for Families," Child Trends, January 4, 2012.
[344] Liebman Supplemental Report, ¶¶ 78–79.
[345] NAMCS Survey Data.
[346] Liebman Supplemental Report, ¶ 14.

costs. From an economic perspective, the only abatement costs that Defendants should be responsible for are the additional costs required to abate negative consequences resulting from Defendants' alleged misconduct. Professor Liebman's analysis fails to calculate these costs.

2. Assumptions Underlying Professor Liebman's Abatement Cost Estimates

193. Beyond the conceptual problems discussed above, Professor Liebman's analysis is unreliable—his cost estimates are crucially dependent on unsupported and unverifiable assumptions about the evolution of treatment needs in the Plaintiff Counties over the next 15 years. Professor Liebman acknowledges that "it is possible that the epidemic will evolve in ways that either reduce or increase the need for resources relative to [his] primary estimates," and purports to provide an economist's solution to this—"a range of estimates for lower cost and higher cost scenarios."[347] Yet, Professor Liebman's low case and high case scenarios are based on just as unsubstantiated assumptions as his base case scenario thereby undermining the scientific validity of his entire analysis.

194. To begin with, only five out of the 19 programs included in Professor Liebman's analysis contemplate more than a single scenario.[348] For the other 14 programs, including the third largest program that would provide welfare services to children purportedly impacted by the opioid crisis, Professor Liebman presents only one set of estimates for a wide range of intangible inputs: required number of social workers, family advocates, trauma counselors, staff to recruit foster families, number of children that require placement in foster or institutional care, number of children that require in-home services, as well as all associated expenditures for the next 15 years. Further, the key assumption underpinning each of these inputs is Professor Liebman's reliance on Professor Cutler's estimate for the share of "opioid-related" removals of children from their homes. As discussed above, not only is there no evidence that this share is actually "opioid-related," but it is also derived from a single data point in 2015, which Professor Cutler

[347] Liebman Supplemental Report, ¶ 20.
[348] Liebman Supplemental Report, corrected Appendix D.

then "forecasts" to 2017.[349] Professor Liebman in turn takes Professor Cutler's 2017 "forecast" and assumes it will still be applicable for the next 15 years—from 2020 through 2034.[350]

195. Even for the five programs where Professor Liebman contemplates more than a single scenario, both his primary and alternative scenarios lack empirical support. Specifically, the costs of all five of these programs depend crucially on Professor Liebman's estimates for how many people will be receiving treatment for addiction and substance abuse in the Plaintiff Counties for the next 15 years. To construct this future series, Professor Liebman makes the following assumptions about the evolution of this treatment population: (1) the treatment population in 2020 will reflect the combined prescription OUD and HUD prevalence Professor McGuire estimates for 2016; (2) the treatment population will grow at a constant rate until 2023, at which point it will have doubled; (3) in the base case, the treatment population will remain constant thereafter; (4) in the low case, the treatment population will decline by one third between 2025 and 2034 at a constant annual rate; and (5) in the high case, the treatment population will increase by one third between 2025 and 2034 at a constant annual rate.[351]

196. Professor Liebman does not offer support for any of these assumptions except to state that he "understand[s] that the Expert Report of Anna Lembke explains that an effective Abatement Plan could expand its reach in this way by 2024."[352] Dr. Lembke in turn opines that "[w]ith an aggressive infusion of resources and efforts […] it would be reasonable that within four years the number of Bellwether individuals with OUD who receive substance abuse treatment services within a year could double."[353] Yet, she provides no support for her opinion of what "could" happen or even quantifies the likelihood of it happening. Despite this, Professor Liebman assumes that this would occur with 100 percent certainty—all of his scenarios, primary and alternative alike, contemplate doubling of the treatment population by 2023. Furthermore, all of his scenarios, including his low case scenario, contemplate that the size of the treatment population in each year between 2024 and 2034 will remain at least 33 percent higher than Professor Liebman's estimate for the size of the treatment population in 2020.[354] Professor

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[349] Cutler Report, ¶ 44.
[350] Cutler Report, ¶ 44; Liebman Supplemental Report, corrected Appendix D, p. 3.
[351] Liebman Supplemental Report, corrected Appendix D.
[352] Liebman Supplemental Report, ¶ 42.
[353] Expert Report of Anna Lembke, M.D., March 25, 2019, ¶ 17.
[354] Liebman Supplemental Report, corrected Appendix D.

Liebman offers no basis to support this—even Dr. Lembke's opinion for what "could" happen does not extend beyond the next four years.

197. Moreover, available data from Ohio contradicts Professor Liebman's assumption about the evolution of substance abuse treatment needs in the Plaintiff Counties. Specifically, the TEDS-A data provide information on individual admissions for prescription OUD or HUD treatment in Ohio treatment facilities that receive federal funding. According to these data, the number of prescription OUD and HUD admissions peaked in 2009 and have been generally declining since then, with 2016 figures being 23 percent lower than the peak in 2009. Furthermore, in every year since 2006 (the start of the putative damages period), 63–70 percent of the admissions involved a patient who received treatment not only for prescription OUD or HUD, but also for another non-opioid substance.[355] Hence, these data not only undermine Professor Liebman's assumption about the growth of the population that would be treated for prescription OUD or HUD in the future, but also undermine the notion that the majority of this population would not have been in treatment but for Defendants' alleged misconduct.[356]

198. In fact, Professor Liebman's assumptions are undermined not only by available data but also by the abatement cost methodology of one of Plaintiffs' epidemiology experts, Dr. Alexander. Unlike Professor Liebman's analysis, Dr. Alexander's analysis seeks to exclude individuals suffering from HUD if their first use of heroin predated any use of prescription opioids.[357] Similarly, unlike Professor Liebman, Dr. Alexander attempts to avoid double counting due to concurrent HUD and prescription OUD and appears to exclude 60 percent of the HUD population.[358] That said, Dr. Alexander's analysis suffers from a number of flaws, as discussed below.

199. Such differences between his analysis and Professor Liebman's are informative as they illustrate the unreliability of assumptions about future inputs underlying any abatement cost calculations. In fact, the Pitt et al. (2018) study, which serves as the basis for Professor Liebman's prescription OUD/HUD prevalence estimates, clearly acknowledges the limitations in

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[355] TEDS-A.

[356] Professor Liebman's assumption about population growth is further undermined by his own notes from meetings with officials in the Plaintiff Counties. During a meeting on July 10, 2018, Summit County officials revealed that overdose deaths have decreased and that they currently have space in residential programs. *See* Meeting with Summit County and Akron Meeting Minutes, July 10, 2018.

[357] Alexander Supplemental Report, "MAT Model 2.0 V51.xlsm."

[358] Alexander Supplemental Report, "MAT Model 2.0 V51.xlsm."

any abatement plan for the opioid crisis, particularly a long-term one such as Professor Liebman's:

> Our analysis has several limitations. First, the drivers behind the opioid epidemic are dynamic, nonlinear, and uncertain. Although we tested the impact of each policy on multiple potential models of the current state, the epidemic continues to change and may be substantially different in just 5 years.[359]

200. More fundamentally, the assumptions employed by Professor Liebman imply that a number of his contemplated abatement programs are ineffective. Indeed, in deposition, Professor Liebman conceded that he did not attempt to measure any impact that implementing any of the categories in his abatement programs might have.[360] Except for five programs—the two treatment programs (with and without MAT), the treatment referrals program, the naloxone kit program, and the syringe exchange program—none of the other 14 programs contemplate any reduction in the target population.[361] This is true even for programs such as the media campaign, the medical provider education and outreach, the drug disposal program, and the law enforcement interventions program, all programs whose size would be expected to decrease over time if at all effective.[362] There is no empirical or logical support for the notion that local governments or any private entity should spend billions of dollars over more than a decade on programs that do not actually achieve their goal of helping abate the problem to any measurable degree. To seek abatement cost damages that do not abate anything does not make economic sense.

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[359] Alison L. Pitt et al., "Modeling Health Benefits and Harms of Public Policy Responses to the US Opioid Epidemic," *American Journal of Public Health* 108, 2018, no. 10, pp. 1394–400 at p. 1399.
[360] Liebman Deposition, 110:8–14.
[361] Liebman Supplemental Report, corrected Appendix D.
[362] Liebman Supplemental Report, corrected Appendix D.

B. Review of Dr. Alexander's Analysis and Opinions

201. Dr. Alexander presents 15 categories of programs and associated cost estimates that would purportedly abate the opioid crisis on a national level for 10 years.[363] As discussed in greater detail below, Dr. Alexander's analysis suffers from a number of flaws including the fact that it is only a national analysis and not in any way tailored to the circumstances of the Plaintiff Counties.[364] In addition, Dr. Alexander's method of calculating national abatement costs is unreliable because it depends in large part on unsupported assumptions. And, like Professor Liebman, Dr. Alexander fails to identify and isolate the incremental abatement costs required due to any alleged misconduct by Defendants.

1. Scope of Dr. Alexander's Abatement Costs

202. Dr. Alexander fails to provide any evidence that the costs of his national abatement programs are due to any alleged misconduct by Defendants. Dr. Alexander's abatement program covers the entire opioid crisis. As discussed above, the only abatement costs that Defendants should be responsible for are the additional costs required to abate negative consequences resulting from Defendants' alleged misconduct. Dr. Alexander does not attempt to isolate the share of abatement costs that address harms due to Defendants actions. Further, to the extent there would have been opioid-related harms in the absence of Defendants' alleged misconduct, these abatement programs might have been implemented in the but-for world. If so, these abatement programs may have been sufficient to address at least some of the additional harms due to Defendants' alleged misconduct without additional costs, or may have lowered the cost of addressing such additional harms. Thus, abatement costs due to Defendants' alleged misconduct are only those costs beyond the amount that would have been spent by abatement programs but for Defendants' alleged misconduct, *i.e.*, incremental costs.

203. Similar to Professor Liebman, Dr. Alexander's model includes programs that are focused on prevention rather than abatement (*e.g.*, Adolescent Interventions). As discussed above,

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[363] In his April 17, 2019 update to his supplemental report, Dr. Alexander for the first time includes three new "scenarios" for calculating national abatement cost estimates. Dr. Alexander provides no guidance on which scenario he considers to be most reliable or realistic. *See* Update to the Supplemental Expert Report and Production of G. Caleb Alexander, MD, MS, April 17, 2019, pp. 2–3.

[364] Alexander Supplemental Report, ¶¶ 176–180.

prevention programs should be in place regardless of whether a community is experiencing a drug-related crisis.

2. Dr. Alexander's Application of a National Abatement Model to the Plaintiff Counties

204. As noted above, Dr. Alexander provides a national estimate of abatement costs. He acknowledges that "the exact costs of abatement . . . will depend upon the population requiring services and the programs in existence in each jurisdiction," and that he has "not conducted any detailed assessment of the specific [abatement] costs within Cuyahoga and Summit Counties," but provides "one proxy" for potentially extrapolating his national estimates to the Plaintiff Counties based on 2017 opioid overdose death rates.[365]

205. There are significant limitations in using a national model to estimate abatement costs for the Plaintiff Counties—which Dr. Alexander readily admits.[366] A number of factors drive opioid use, abuse, and death over time, and Dr. Alexander's analysis does not capture any features specific to the Plaintiff Counties except their purported share of opioid overdose deaths in a single year. Specifically, Dr. Alexander estimates that in 2017, opioid-related deaths in the Plaintiff Counties accounted for 1.5 percent of national opioid-related deaths. He then applies this 1.5 percent to the national abatement costs to approximate abatement costs in the Plaintiff Counties.[367] As evidence of the lack of reliability of local estimates based solely on the share of national opioid overdose deaths, one need look no further than Dr. Alexander's own parameter values. For example, Dr. Alexander's analysis assumes a national mass media target population of 150 million.[368] Applying his percentage of the Plaintiff Counties' purported share of national abatement costs (1.5 percent) to the national mass media target population yields a population of 2.25 million for the Plaintiff Counties. However, according to U.S. Census data, the entire population of the Plaintiff Counties in 2018 was only 1.79 million.[369]

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[365] Alexander Supplemental Report, ¶¶ 175, 180; Alexander Deposition, 136:4–8.
[366] *See*, *e.g.*, Alexander Supplemental Report ¶ 180; Alexander Deposition, 163:1–165:22.
[367] Alexander Supplemental Report, ¶ 180.
[368] Alexander Supplemental Expert Report, "All Redress Models 17APR19V14.xlsx."
[369] Annual Estimate of the Resident Population: July 1, 2018. U.S. Census Bureau, Population Division.

206. During his deposition Dr. Alexander admitted that his model "is a national model, not a local model" and that other Plaintiffs' experts are "focused on estimating the specific costs in Cuyahoga and Summit Counties."[370] To the extent that Dr. Alexander does offer an opinion regarding specific abatement costs for the Plaintiff Counties based on his national estimates, I am prepared to discuss the numerous additional limitations inherent in his methodology.

3. Dr. Alexander's Methodology of Calculating National Abatement Cost Estimates

207. Dr. Alexander's national abatement analysis is unreliable because his cost estimates are dependent on unsupported and unverifiable assumptions. At least 20 percent of the parameters informing his cost estimates are based on unsubstantiated assumptions, which undermines the scientific validity of his entire analysis.[371] As Dr. Alexander acknowledged, it is reasonable to assume that another expert using his model is likely to make different assumptions and, if so, that expert's cost estimates would differ from those offered by Dr. Alexander.[372]

208. For a subset of his abatement categories, Dr. Alexander models how specific populations within the opioid crisis will purportedly change in size from 2018–2028 based on his "APOLLO model."[373] The APOLLO model is the product of Dr. Alexander's consulting firm, Monument Analytics.[374] It has not been used in academic research nor been subject to any peer-review through the publication process.[375] Indeed, Dr. Alexander admitted to not having used this type of epidemiologic model prior to his work in this litigation.[376] Without subjecting the APOLLO model to the scrutiny of other experts in the field, there is no way to ensure the validity of the model or the cost estimates that derive from it.

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[370] Alexander Deposition, 272:25–273:1, 260:11–264:09, 192:12–16 ("I was not asked to design an abatement program for these counties.")
[371] Based on calculating the share of parameters whose source is "Assumed" in "Monument Analytics Abatement Sources 17APR19V10.xlsx."
[372] Alexander Deposition, 199:20–200:16.
[373] Alexander Supplemental Report, "MAT Model 2.0 V51.xlsx."
[374] Alexander Deposition, 117:7–10.
[375] Alexander Deposition, 105:25–106:3, 117:11–13.
[376] Alexander Deposition, 104:12–14.

209. The APOLLO model attempts to "track key opioid populations including prescription drug users, heroin users, and heroin users that started with prescription drugs, as they transition in and out of treatment under a variety of policy interventions and economic assumptions."[377] The validity of Dr. Alexander's approach rests upon the ability of the model to make reliable predictions about future population sizes. Based on his produced materials, it does not appear that Dr. Alexander has tested whether his methods generate reliable predictions into the future. In the absence of such tests, Dr. Alexander's method of prediction remains unverified.

210. As discussed above with respect to Professor Liebman's abatement analysis, the assumptions employed by Dr. Alexander imply that a number of his contemplated abatement programs are ineffective, which makes no economical or logical sense. Specifically, in seven of his abatement categories, Dr. Alexander utilizes a constant population size from 2018 to 2028, and explores no impacts of abatement on these population sizes.[378] This includes programs such as the mass media campaign, academic detailing, drug disposal program, and law enforcement interventions program, all programs whose size would be expected to decrease over time if effective. Further, for those programs that are impacted by abatement in Dr. Alexander's model, he provides no support for the size of the impact he assumes.

Iain Cockburn, Ph.D.

[377] Alexander Supplemental Report, "MAT Model 2.0 V51.xlsx."
[378] Alexander Expert Report Update, "All Redress Models 17APR19V14.xlsx."

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I. EDUCATION

Undergraduate

Queen Mary College, University of London, B.Sc.(Econ) Hons 1st Class, 1984.

Graduate

Harvard University, A.M. Economics, 1987

Harvard University, Ph.D. Economics, 1990

Doctoral Thesis

Essays on the Analysis of Technical Change. Supervisor: Zvi Griliches, Paul M. Warburg Professor of Economics, Harvard University.

Academic Awards Prior to Final Degree

Kennedy Scholar, 1984

Alfred P. Sloan Doctoral Dissertation Fellowship, 1988

II. PROFESSIONAL EMPLOYMENT

July 2016 –	*Chair*, Strategy and Innovation Department, Questrom School of Business, Boston University
September 2013 – June 2014	*Visiting Scholar*, Technology, Innovation, and Entrepreneurship Department, MIT Sloan School of Management.
July 2011 –	*Richard C. Shipley Professor in Management*, Questrom School of Business, Boston University
July 2010 – July 2011	*Professor of Strategy and Innovation*, School of Management, Boston University
September 1999 – July 2010	*Professor of Finance and Economics*, School of Management, Boston University
July 1998 – July 2000	*VanDusen Professorship in Business Administration*, Faculty of Commerce, University of British Columbia
July 1997 – July 1998	*Associate Professor with Tenure*, Faculty of Commerce, University of British Columbia.
July 1996 – June 1997	*Visiting Scholar*, Department of Economics, Harvard University.
July 1993 – December 1993	*Visiting Scholar*, Economics, Finance, and Accounting Department, MIT Sloan School of Management.
July 1989 – June 1997	*Assistant Professor*, Faculty of Commerce, University of British Columbia.

III. PROFESSIONALLY RELATED ACTIVITIES

Awards

UBC Faculty of Commerce Research Excellence Award, 1997
UBC Commerce Graduate Society Teaching Award, 1997
BU School of Management, 2nd Year MBA Teacher of the Year, 2004-5
Everett W. Lord Distinguished Faculty Scholar, BU School of Management 2004 - 2011
Molly McCombe and T.J. Callahan Faculty Research Award, 2016
John R. Russell Excellence in Teaching Award, BU Executive MBA Program, 2018

Research Interests

Economics of Technical Change, Intellectual Property, Competitive Strategy, Industrial Organization, Information Technology, Pharmaceutical and Health Economics, Applied Econometrics

Teaching

UBC Undergraduate classes: Corporate and Industry Analysis; Government and Business

UBC MBA classes: Technology Strategy and Policy; Business Policy; Competition in High Technology Industries; Intellectual Property and Business Strategy; Strategic Partnering

BU MBA/EMBA classes: Competition in High Technology Industries; Intellectual Property and Business Strategy; Managing Global Customers, Competencies and Capabilities; Competition, Innovation, and Strategy; Licensing and Partnering; IP Strategies for Life Sciences and Technology; Industry and Competitive Analysis; Competitive Strategy

BU PhD classes: Seminar in Strategy and Innovation

Executive Education seminars: Hanjung Programme (UBC); Posco Programme (UBC); Strategic Planning in High Tech Environments (UBC); IBM Advanced Program for Client Executives (BU)

Committees

Steering Committee, Government Industry Partnerships for the Development of New Technologies, National Research Council, Washington DC, 1998 – 2000

Scientific Committee, European Union INNOVPROD Research Network 1996 - 1999

Refereeing

Journal of Health Economics, Journal of Political Economy, American Economic Review, RAND Journal of Economics, Journal of the American Statistical Association, Journal of Economics and Management Strategy, Review of Economics and Statistics, Journal of Industrial Economics, Quarterly Journal of Economics, Journal of International Economics, Management Science, Managerial and Decision Economics, Journal of Economic Behavior and Organization, Economic Inquiry, Administrative Science Quarterly, others.

Editorships

Associate Editor, Strategy Department, Management Science, 1997-2000

Coeditor, Journal of Economics and Management Strategy, 1998 – 2005

Editorial Board, Strategy and Organization, 2001 – 2004

Professional Affiliations

Research Associate, National Bureau of Economic Research, Cambridge MA

Member, Conference on Research in Income and Wealth, 2011 -

Associate Member, Faculty of Pharmaceutical Sciences, UBC 1992-1998

Research Director, BU Institute for Technology, Entrepreneurship and Commercialization, 2008 - 2010

Major Research Funding

December 2012	*Evaluating Changes in Pharmaceutical Therapies for Medicare and Other Payers* (Co-PI, Ernst Berndt, Principal Investigator.) National Institute on Aging, R01AG043560, $932,000.
June 2012	*Global Diffusion of New Drugs: Patent Policy, Price Regulation and Health Institutions* (Principal Investigator, Mark Schankerman (LSE) Co-PI.) National Foreign Trade Council Foundation, $508,799
October 2009	*An Experimental Producer Price Index for Clinical Trials* (Principal Investigator; Ernst Berndt, Co-PI). National Science Foundation, SES-0915677, $120,000
October 2008	*Strategic, Economic and Epidemiological Factors Affecting the Changing Allocation of Global Clinical Trials* (Co-PI; Ernst Berndt, Principal Investigator, Howard Golub, Co-PI). Alfred P. Sloan Foundation, $302,000
October 2005	*Harnessing Patent Data for Social Science Research* (Principal Investigator; Bronwyn Hall, Walter Powell, Manuel Trajtenberg, Co-PIs). National Science Foundation, SES-0527657, $599,000
October 2002	*Valuing Mobile Computing* (Principal Investigator; Ernst Berndt (MIT), Co-Investigator). National Science Foundation, SES-0219235, $145,000
April 2002	*Time Series Modeling of Trends in Medication Prescribing* (Co-investigator; Randall Stafford (Stanford), PI). Agency for Healthcare Research and Quality, HS013405, $992,000
August 2000	*Patent Examiner Productivity and Quality* (with Samuel Kortum, BU, and Scott Stern MIT). National Academy of Sciences/NRC, $20,000
October 1998	*Canadian Arthritis Network* (Co-investigator; Tony Cruz, University of Toronto, PI) SSHRC/NSERC National Centers of Excellence Award, $14.5million
July 1998	*Intellectual Property Rights in the Knowledge-Based Economy*, Industry Canada, $25,000
April 1997	*Pharmaceutical Research in the New Environment* (with Rebecca Henderson, MIT) Alfred P. Sloan Foundation and MIT Program on the Pharmaceutical Industry, $120,000.
January 1996	*Hedonic Price Analysis of Drug Therapies for Rheumatoid Arthritis* (with Aslam Anis, UBC) NBER and Bureau of Economic Analysis (US Department of Commerce), $35,000
April 1995	*Public-Private Interaction in Pharmaceutical Research* (with Rebecca Henderson, MIT) Sloan Foundation and MIT Program on the Pharmaceutical Industry, $120,000
July 1994	*Pharmaceutical Pricing*, MIT Program on the Pharmaceutical Industry, $40,000
April 1994	*Innovation and Entrepreneurship* - UBC-SSHRC Entrepreneurship Research Alliance, $130,000
August 1991	*Determinants of Research Productivity in the Pharmaceutical Industry* (with Rebecca Henderson, MIT) Alfred P. Sloan Foundation, Hoffman-La Roche Ltd., Bristol Myers Squibb Inc., Pharmaceutical Manufacturers Association, $170,000

PUBLICATION RECORD

Iain M. Cockburn

A. PUBLICATIONS

Refereed Articles

1. Cockburn, I., J. Lanjouw, and M. Schankerman "Patents and the Global Diffusion of New Drugs." *American Economic Review*, 2016, 106(1):136-164.
2. Cockburn, I. and G. Long "The Importance of Patents to Innovation: Updated Cross-Industry Comparisons with Biopharmaceuticals." *Expert Opinion on Therapeutic Patents*, 2015, 25(7):739-742.
3. Freedman, L. I. Cockburn, and T. Simcoe "The Economics of Reproducibility in Preclinical Research." *PLOS Biology*, 2015, 13(6): e1002165.
4. Berndt, E. and I. Cockburn "Price Indexes for Clinical Trial Research: A Feasibility Study." *Monthly Labor Review*, June 2014.
5. Agrawal, A., I. Cockburn, L. Zhang "Deals Not Done: Sources of Failure in the Market for Ideas." *Strategic Management Journal*, 2015, 36(7):976-986.
6. Berndt, E. and I. Cockburn "The Hidden Cost of Low Prices: Limited Access to New Drugs in India." *Health Affairs*, 2014, 33(9):1567-1575.
7. Agrawal, A. Cockburn, I., Galasso, A. and A. Oettl "Why are some regions more innovative than others? The role of small firms in the presence of large labs*." Journal of Urban Economics*, 2014, 81(1):149–165.
8. Müller, E., I. Cockburn, and M. MacGarvie, "Access to intellectual property for innovation: Evidence on problems and coping strategies from German firms." *Research Policy*, 2013, 42(2):529-541.
9. Kleis, L., P. Chwelos, R. Ramirez and I. Cockburn "Information Technology and Intangible Output: The Impact of IT Investment on Innovation Productivity." *Information Systems Research*, 2012, 23:42-59.
10. Berndt, E., N. Blalock and I. Cockburn "Diffusion of New Drugs in the Post-TRIPs Era." *International Journal of the Economics of Business*, 2011, 18(2):203-224.
11. Cockburn, I., and M. MacGarvie "Entry and Patenting in the Software Industry." *Management Science*, 2011, 57(5):915-933.
12. Bollyky, T., I. Cockburn and E. Berndt "Bridging the gap: improving clinical development and the regulatory pathways for health products for neglected diseases." *Clinical Trials*, 2010, 7(6):719-34.
13. Cockburn, I. and S. Stern "Finding the Endless Frontier: Lessons from the Life Sciences Innovation System for Technology Policy." *Capitalism and Society*, 2010, 5(1), article 1.
14. Wagner, S. and I. Cockburn "Patents and the Survival of Internet-related IPOs." *Research Policy*, 2010, 39(2):214-228.
15. Cockburn, I., M. MacGarvie, and E. Müller "Patent Thickets, Licensing and Innovative Performance." *Industrial and Corporate Change*, 2010, 19(3):899-925.
16. Agrawal, A., I. Cockburn and C. Rosell "Not Invented Here: Innovation in Company Towns." *Journal of Urban Economics*, 2010, 67(1):78-89.
17. Cockburn, I., and M. MacGarvie "Patents, Thickets and the Financing of Early-Stage Firms: Evidence from the Software Industry." *Journal of Economics and Management Strategy*, 2009, 18(3):729-773.

18. Chwelos, P., E. Berndt, and I. Cockburn "Faster, Smaller, Cheaper: An Hedonic Price Analysis of PDAs." *Applied Economics*, 2008, 40(22):2839-56.

19. Agrawal, A., I. Cockburn, and J. McHale "Gone But Not Forgotten: Labor Flows, Knowledge Spillovers, and Enduring Social Capital." *Journal of Economic Geography*, 2006, 6(5):571-591.

20. Berndt, E., I. Cockburn, and K. Grépin "The Impact of Incremental Innovation in Biopharmaceuticals: Drug Utilization in Original and Supplemental Indications." *Pharmacoeconomics*, 2006, 24(Suppl. 2):69-83.

21. Grabowski, H., I. Cockburn and G. Long "The Market for Follow-on Biologics: How Will It Evolve?" *Health Affairs*, 2006, 25(5):1291-1301.

22. Furman, J., M. Kyle, I. Cockburn, and R. Henderson "Public and Private Spillovers, Location and the Productivity of Pharmaceutical Research." *Annales d'Economie et de Statistique*, 2005, 79/80:165-188.

23. Cockburn, I. "The Changing Structure of the Pharmaceutical Industry." *Health Affairs*, 2004, 23(1):10-22.

24. Stafford, R., C. Furberg, S. Finkelstein, I. Cockburn, T. Alehegn, and J. Ma "The Impact of Clinical Trial Results On National Trends in Alpha-Blocker Prescribing, 1996-2002." *Journal of the American Medical Association*, 2004, 291:54-62.

25. Agrawal, A., and I. Cockburn "The Anchor Tenant Hypothesis: Exploring the Role of Large, Local, R&D-Intensive Firms in Regional Innovation Systems." *International Journal of Industrial Organization*, 2003, 21(9):1217-1433.

26. Ma J., R. Stafford, I. Cockburn, and S. Finkelstein "A Statistical Analysis of the Magnitude and Composition of Drug Promotion in the U.S." *Clinical Therapeutics*, 2003; 25(5):1503-1517.

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28. Cockburn, I. and R. Henderson "Scale and Scope in Drug Development: Unpacking the Advantages of Size in Pharmaceutical Research." *Journal of Health Economics*, 2001, 20(6):1033-1057.

29. Lanjouw, J. and I. Cockburn "New Pills for Poor People? Empirical Evidence After GATT." *World Development*, February 2001, 29(2):265-289.

30. Cockburn, I., R. Henderson, and S. Stern, "Untangling the Origins of Competitive Advantage." *Strategic Management Journal*, December 2000, 21(10-11):1123-1145. Reprinted in *The SMS Blackwell Handbook of Organizational Capabilities: Emergence, Development, and Change*, edited by Constance Helfat, Strategic Management Society Book Series. Malden, MA, 2003.

31. Cockburn, I., H. Bailit, E. Berndt, and S. Finkelstein "Loss of Work Productivity Due to Illness and Medical Treatment." *Journal of Occupational and Environmental Medicine*, November 1999: 41(11):1-6.

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33. Berndt, E., I. Cockburn, D. Cocks, A. Epstein, and Z. Griliches "Prescription Drug Prices for the Elderly." *Monthly Labor Review*, September 1998, 121(9):23-34.

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35. Wang, P., I. Cockburn, and M. Puterman "Analysis of Patent Data - A Mixed Poisson Regression Approach." *Journal of Business and Economic Statistics*, 1998, 16(1):27-41.

36. Ellison, S., I. Cockburn, Z. Griliches, and J. Hausman "Characteristics of Demand for Pharmaceutical Products: An Examination of Four Cephalosporins." *RAND Journal of Economics*, 1997, 28(3):426-446.

37. Berndt, E., I. Cockburn, and Z. Griliches "Pharmaceutical Innovations and Market Dynamics: Tracking Effects on Price Indexes for Anti-Depressant Drugs." *Brookings Papers on Economic Activity: Microeconomics*, 1996, 1:133-188.

38. Henderson, R. and I. Cockburn "Scale, Scope, and Spillovers: Determinants of Research Productivity in the Pharmaceutical Industry." *RAND Journal of Economics*, 1996, 27(1):32-59.

39. Wang, P., M. Puterman, N. Le, and I. Cockburn "Mixed Poisson Models with Covariate-Dependent Rates." *Biometrics*, 1996, 52:381-400.

40. Amit, R., E. Muller, and I. Cockburn "Opportunity Costs and Entrepreneurial Activity." *Journal of Business Venturing*, 1995, 10(2):95-106. Reprinted in *Foundations of Entrepreneurship*, edited by S. Shane, Edward Elgar, 2000.

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42. Henderson, R. and I. Cockburn "Measuring Competence: Exploring Firm Effects in Pharmaceutical Research." *Strategic Management Journal*, 1994, 15:63-84. Reprinted in *The Nature and Dynamics of Organizational Capabilities*, edited by G. Dosi, R. Nelson, and S. Winter, Oxford University Press, Oxford, 2000, pp. 155-182.

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44. Cockburn, I. and Z. Griliches "Industry Effects and Appropriability Measures in the Stock Market's Valuation of R&D and Patents." *American Economic Review, Papers and Proceedings*, 1988, 78(2):419-423.

Contributions to Edited Volumes

1. Cockburn, I. R. Henderson, and S. Stern "The Impact of Artificial Intelligence on Innovation." Chapter in A. Agrawal, J. Gans, and A. Goldfarb (eds.) *The Economics of Artificial Intelligence*, University of Chicago Press for the National Bureau of Economic Research, Cambridge MA, forthcoming.

2. Aitken, M., E. Berndt, B. Bosworth, I. Cockburn, R. Frank, M. Kleinrock, and B. Shapiro "The Regulation of Prescription Drug Competition and Market Responses: Patterns in Prices and Sales Following Loss of Exclusivity." Chapter in A. Aizcorbe, C. Baker, E. Berndt, and D. Cutler, eds. *Measuring and Modeling Health Care Costs*, University of Chicago Press for the National Bureau of Economic Research, Cambridge MA, forthcoming.

3. Cockburn, I. S. Stern, and J. Zausner "Finding the Endless Frontier: Lessons from the Life Sciences Innovation System for Energy R&D." Chapter in R. Henderson and R. Newell, eds. *Accelerating Energy Innovation: Lessons from Multiple Sectors*. University of Chicago Press for the National Bureau of Economic Research, Cambridge MA, 2011.

4. Cockburn, I. and M. Slaughter "The Global Location of Biopharmaceutical Knowledge Activity: New Findings, New Questions," Chapter in J. Lerner, and S. Stern (eds.) *Innovation Policy and the Economy*, Volume 10. University of Chicago Press for the National Bureau of Economic Research, Cambridge MA, 2009. pp. 129-157

5. Cockburn, I. "Intellectual Property Rights and Pharmaceuticals: Challenges and Opportunities for Economic Research." In *The Economics of Intellectual Property. Suggestions for Further Research in Developing*

Countries and Countries with Economies in Transition. World Intellectual Property Organization, Geneva. 2009.

6. Cockburn, I. "Pharmaceuticals." Chapter in D. Mowery, J. Macher and S. Merrill (eds.) *Globalization of Innovation: U.S. Firms Competing in a New World.* National Academies Press, Washington DC. 2008. pp. 207-230.
7. Cockburn, I. "Is the Pharmaceutical Industry in a Productivity Crisis?" Chapter in A. Jaffe, J. Lerner, and S. Stern (eds.) *Innovation Policy and the Economy*, Volume 7. MIT Press for the National Bureau of Economic Research, Cambridge MA. 2007. pp. 1-32.
8. Cockburn, I. "Blurred Boundaries: Tensions Between Open Scientific Resources and Commercial Exploitation of Knowledge in Biomedical Research." Chapter in D. Foray and B. Kahin (eds.) *Advancing Knowledge and the Knowledge Economy*. MIT Press, 2006.
9. Cockburn, I. "*State Street* Meets the Human Genome Project: Intellectual Property and Bioinformatics." Chapter in R. Hahn (ed.) *Intellectual Property Rights in Frontier Industries: Biotechnology and Software*, AEI-Brookings Press, Washington DC, 2005.
10. Lacetera, N., I. Cockburn, and R. Henderson "Do Firms Change Capabilities by Hiring New People? A study of the Adoption of Science-based Drug Discovery." Chapter in J. Baum and A. McGahan (eds.) *Business Strategy over the Industry Lifecycle: Advances in Strategic Management Volume 21*, pp 133-159, JAI-Elsevier Science, New York, 2004.
11. Cockburn, I. "O Brave New Industry That Has Such Patents In It! Reflections on the Economics of Genome Patents." Chapter in F. S. Keiff (ed.) *Perspectives on Properties of the Human Genome Project*, Academic Press, Boston, 2004.
12. Cockburn, I., S. Kortum, and S. Stern "Are All Patent Examiners Equal? Examiners, Patent Characteristics and Litigation Outcomes." Chapter in W. Cohen and S. Merrill (eds.) *Patents in the Knowledge-based Economy*, National Academies Press, Washington DC, 2003. pp. 19-52.
13. Cockburn, I. and R. Henderson "Publicly Funded Science and the Productivity of the Pharmaceutical Industry." Chapter in A. Jaffe, J. Lerner, and S. Stern (eds.) *Innovation Policy and the Economy*, Volume 1. MIT Press for the National Bureau of Economic Research, Cambridge MA, 2001. pp 1-34.
14. Cockburn, I. and A. Anis "Hedonic Analysis of Arthritis Drugs." Chapter in E. Berndt and D. Cutler (eds.) *Medical Care Output and Productivity*, University of Chicago Press, Chicago IL, 2001. pp. 439-462.
15. Cockburn, I. and P. Chwelos "Intellectual Property Rights and the Transition to the Knowledge-based Economy." Chapter in L. Lefebvre, E. Lefebvre, and P. Mohnen (eds.) *Doing Business in the Knowledge-based Economy*, Kluwer Academic Publishers, Boston MA, 2001.
16. Cockburn, I., R. Henderson, L. Orsenigo, and G. Pisano "Pharmaceuticals and Biotechnology." Chapter in D. Mowery (ed.) *U.S. Industry in 2000: Studies in Competitive Performance*, National Research Council, Washington DC, 1999, pp. 363-398.
17. Cockburn, I. and R. Henderson "The Economics of Drug Discovery." Chapter in Ralph Landau, Basil Achilladelis and Alexander Scriabine (eds.) *Pharmaceutical Innovation*, Chemical Heritage Press, Philadelphia PA, 1999, pp. 308-331.
18. Berndt, E., I. Cockburn, D. Cocks, A. Epstein, and Z. Griliches "Is Price Inflation Different for the Elderly? An Empirical Analysis of Prescription Drugs." Chapter in A. Garber (ed.) *Frontiers in Health Policy Research*, MIT Press, Cambridge MA, 1998.
19. Henderson, R. and I. Cockburn "Taille de la Firme et Productivité de la Recherche." Chapter in S. Jacobzone (ed.) *La santé: Trajectoires d'Avenir*, INSEE, Paris, 1997.

20. Henderson, R. and I. Cockburn "The Determinants of Research Productivity in Ethical Drug Discovery." Chapter in R. Helms (ed.) *Competitive Strategies in the Pharmaceutical Industry*, American Enterprise Institute, Washington DC, 1996.
21. Griliches, Z. and I. Cockburn "Generics and the Producer Price Index for Pharmaceuticals." Chapter in R. Helms (ed.) *Competitive Strategies in the Pharmaceutical Industry*, American Enterprise Institute, Washington DC, 1996.

Working Papers, Manuscripts etc.

1. Cockburn, I., J. Lanjouw, and M. Schankerman "Patents and the Global Diffusion of New Drugs." NBER Working Paper No. 20492, September 2014.
2. Agrawal, A., I. Cockburn, and L. Zhang "Deals Not Done: Sources of Failure in the Market for Ideas." NBER Working Paper No. 19679, November 2013.
3. Aitken, M., E. Berndt, B. Bosworth, I. Cockburn, R. Frank, M. Kleinrock, and B. Shapiro "The Regulation of Prescription Drug Competition and Market Responses: Patterns in Prices and Sales Following Loss of Exclusivity." NBER Working Paper No. 18487, October 2013.
4. Berndt, E. and I. Cockburn "Price Indexes for Clinical Trial Research: A Feasibility Study." NBER Working Paper No. 18918, March 2013.
5. Agrawal, A. Cockburn, I., Galasso, A. and A. Oettl "Why are Some Regions More Innovative than Others? The Role of Firm Size Diversity." NBER Working Paper No. 17793, January 2012.
6. Müller, E. Cockburn, I. and MacGarvie, M. "Access to Intellectual Property for Innovation: Evidence on Problems and Coping Strategies from German Firms." TILEC Discussion Paper No. 2010-042, December 2010.
7. Agrawal, A., Cockburn, I. and C. Rosell "Not Invented Here: Innovation in Company Towns." NBER Working Paper No. 15437, October 2009.
8. Grabowski, H., I. Cockburn, G. Long, R. Mortimer "Data Exclusivity Periods and Next Generation Improvements to Innovator Biologics: Key Issues." Working Paper 2009-05, Department of Economics, Duke University. April. 2009.
9. Cockburn, I., M. MacGarvie, and E. Müller "Patent Thickets, Licensing and Innovative Performance." ZEW Center for European Economic Research Working Paper No. 08-101. November 2008.
10. Kleis, L., P. Chwelos, R. Ramirez and I. Cockburn "Information Technology and Intangible Output: The Impact of IT Investment on Innovation Productivity." Working Paper, Sauder School of Business.
11. Cockburn, I. and M. MacGarvie "Patents, Thickets and the Financing of Early-Stage Firms: Evidence from the Software Industry." NBER Working Paper No. 13644, November 2007.
12. Grabowski, H., I. Cockburn, G. Long, R. Mortimer, and S. Johnson "The Effect on Federal Spending of Legislation Creating a Regulatory Framework for Follow-on Biologics: Key Issues and Assumptions." Working Paper 2007-09, Department of Economics, Duke University. August 2007.
13. Cockburn, I. and S. Wagner "Patents and the Survival of Internet-related IPOs." NBER Working Paper No. 13146, June 2007.
14. Cockburn I. "Is the Market for Technology Working Well? Obstacles to Licensing and Ways to Overcome Them." Conference Paper, Conference on Economics of Technology Policy, Monte Verità, June 2007.

15. Cockburn, I. "Global Innovation in the Pharmaceutical Industry." Conference Paper, Conference on Globalization of Innovation: Emerging Trends in IT, Biopharma and Financial Services, National Academy of Sciences, Washington DC, April 2007.

16. Cockburn, I. and M. MacGarvie "Entry, Exit, and Patenting in the Software Industry." NBER Working Paper No. 12563, October 2006.

17. Furman, J., M. Kyle, I. Cockburn, and R. Henderson "Public and Private Spillovers, Location and the Productivity of Pharmaceutical Research." NBER Working Paper No. 12509, September 2006.

18. Hausman, J. Berndt, E., P. Chwelos, and I. Cockburn "Measurement of the Change in Economic Efficiency from New Production Introductions." Mimeo, MIT, August 2005.

19. Chwelos, P., E. Berndt, and I. Cockburn "Faster, Smaller, Cheaper: An Hedonic Price Analysis of PDAs." NBER Working Paper No. 10746, September 2004.

20. Agrawal, A., I. Cockburn, and J. McHale "Gone But Not Forgotten: Labor Flows, Knowledge Spillovers, and Enduring Social Capital." NBER Working Paper No. 9950, September 2003.

21. Agrawal, A. and I. Cockburn "University Research, Industrial R&D, and the Anchor Tenant Hypothesis." NBER Working Paper No. 9212, September 2002.

22. Cockburn, I., S. Kortum, and S. Stern "Are All Patent Examiners Equal? The Impact of Examiner Characteristics on Patent Statistics and Litigation Outcomes." NBER Working Paper No. 8980, June 2002.

23. Cockburn, I., R. Henderson, and S. Stern "Untangling the Origins of Competitive Advantage." MIT Sloan School of Management Working Paper No. 4109, March 2000.

24. Lanjouw, J. and I. Cockburn "Do Patents Matter? Empirical Evidence After GATT." NBER Working Paper No. 7495, January 2000.

25. Cockburn, I., R. Henderson, and S. Stern "The Diffusion of Science Driven Drug Discovery: Organizational Change in Pharmaceutical Research." NBER Working Paper No. 7359, September 1999.

26. Finkelstein, S., I. Cockburn, H. Bailit, J. Verner, K. Haver, and E. Berndt "Lost Work Productivity and Absenteeism Among Parents of Children with Asthma." MIT Program on the Pharmaceutical Industry, WP #57-00, November 1999.

27. Cockburn, I., R. Henderson, and S. Stern "Balancing Incentives: The Tension Between Basic and Applied Research." NBER Working Paper No. 6882, January 1999.

28. Cockburn, I. and A. Anis "Hedonic Analysis of Arthritis Drugs." NBER Working Paper No. 6574, May 1998.

29. Cockburn, I. and R. Henderson "Public-Private Interaction and the Productivity of Pharmaceutical Research." NBER Working Paper No. 6018, April 1997.

30. Cockburn, I. and R. Henderson "Exploring Inertia: Organizational Failure and Governance Costs in Pharmaceutical Research." Mimeo, MIT Sloan School of Management, October 1994.

31. Cockburn, I. and R. Henderson "Determinants of Research Productivity in the Pharmaceutical Industry." NYU Center for Japan-US Business and Economic Studies Working Paper No. 174, Nov 1994.

32. Henderson, R. and I. Cockburn "Racing or Spilling? The Determinants of Research Productivity in Ethical Drug Discovery." MIT Sloan School of Management Working Paper No. 3642-93, 1993.

33. Griliches, Z. and I. Cockburn "Generics and New Goods in Pharmaceutical Price Indexes." NBER Working Paper No. 4272, February 1993.

34. Cockburn, I. and M. Frank "Market Conditions and the Retirement of Physical Capital: Evidence from Oil Tankers." NBER Working Paper No. 4194, October 1992.

35. Cockburn, I. "The Demand for Water in Maricopa County." Salt River Project, Phoenix, Arizona, 1985.

Conference Proceedings

1. Cockburn, I. and R. Henderson "Patent Races in Pharmaceutical Research." *Risk and Return in the Pharmaceutical Industry: Papers from the 1996 Pharmaceutical Research Perspectives Conference*, Office of Health Economics, London, 1999.
2. Cockburn, I. and R. Henderson "Public-Private Interaction in Pharmaceutical Research." *Proceedings of the National Academy of Sciences*, 92/93, 12 November 1996, pp. 12725-12730.

Abstracts

1. Cockburn, I. "O brave new industry, that has such patents in it! Reflections on the economic consequences of patenting DNA" *Advances in Genetics*, 2003, 50:385-398.
2. Stafford R., S. Finkelstein, I. Cockburn, C. Furberg, T. Alehegn "National trends in antihypertensive prescribing patterns, 1990-2002." *Journal of General Internal Medicine*, April 2003, 18(Suppl. 1):157-157.
3. Radley, D., R. Stafford, S. Finkelstein, and I. Cockburn "Off-label Prescription Among Outpatient Physicians." AcademyHealth Annual Research Meeting, San Diego, June 2004.
4. Cockburn I., E. Berndt, S. Finkelstein, and H. Bailit "Evaluating the impact of antihistamine use on productivity in the workplace." *Journal of Allergy and Clinical Immunology*, Jan 1999, 103(1):968, Part 2 Suppl. S.

Other

1. Signatory, Brief of Antitrust Economists as *Amici Curiae* before the United States Court of Appeals for the Third Circuit, In Re: Wellbutrin XL Antitrust Litigation, No. 15-3559 & 15-3681 (May 10, 2016).
2. Signatory, Brief of Antitrust Economists as *Amici Curiae* before the United States Court of Appeals for the Third Circuit, In Re: Effexor XR Antitrust Litigation, No. 15-1184 (February 23, 2016).
3. Signatory, Brief of Antitrust Economists as *Amici Curiae* before the United States Court of Appeals for the Third Circuit, In Re: Lamictal Direct Purchaser Antitrust Litigation No. 14-1243 (June 3, 2014).
4. Signatory, Brief of Antitrust Economists as *Amici Curiae* before the Supreme Court, Federal Trade Commission v. Actavis, Inc., et al., No. 12-416 (February 28, 2013).
5. Cockburn, I. "Remarks on Costs of Patent Assertion Entities." FTC/DOJ Patent Assertion Entity Activities Workshop, December 10, 2012.
6. Cockburn, I. "Comment: 'The Confederacy of Heterogeneous Software Organizations and Heterogeneous Developers: Field Experimental Evidence on Sorting and Worker Effort,' by Kevin J. Boudreau and Karim R. Lakhani" in Josh Lerner and Scott Stern (eds.) *The Rate and Direction of Inventive Activity Revisited*, University of Chicago Press, 2012, pp502-505.
7. Cockburn, I. "Comments on Nathan Rosenberg's 'Critical Episodes in the Progress of Medical Innovation'" in D. Foray (ed.) *The New Economics of Technology Policy*, Edward Elgar, 2010.

8. Cockburn, I. “Remarks before the FTC Hearings on the Evolving IP Marketplace.” April 17, 2009.
9. Berneman, L., I. Cockburn, A. Agrawal, S. Iyer “US/Canadian Licensing in 2007-8: Survey Results.” *les Nouvelles,* XLIV(1), pp1-8, March 2009.
10. Cockburn, I. “Remarks Before the Department of Health and Human Services Task Force on Drug Importation.” April 26, 2004.
11. Cockburn, I. “Comments” (Response to Commissioner McClellan’s remarks on international price discrimination in pharmaceuticals.) *Milken Institute Review*, First Quarter 2004, pp. 87-92.
12. Giorganni, S., A. Arora, O. Bjerrum, I. Cockburn, K. Doshi, J. Hughes, L. Orsenigo, I. Osterloh, R. Paoletti, S. Preskorn, E. Weiner “The Stream of Progress.” *Pfizer Journal*, November 2003, IV(2):4-11.
13. Cockburn, I. “Remarks on the Proper Scope of IP Rights in the Post-Genomics Era.” *Boston University Journal of Science and Technology Law*, Winter 2002, 8(1):240-244.
14. Edgell E., K. Gregor, and I. Cockburn “Letter.” *Clinical Therapeutics,* May 1999, 21(5):917-924.
15. Griliches, Z. and I. Cockburn “Generics and new goods in pharmaceutical price indexes: Reply.” *American Economic Review,* Sep 1997, 87(4):768-768.

B. SELECTED SEMINAR AND CONFERENCE PRESENTATIONS

1. Discussant remarks: "Data Opportunities and AI" NBER Conference on Economics of Artificial Intelligence, Toronto, September 2018
2. Discussant remarks: Frielich "The Problem of Fictional Data in Patents" NBER Summer Institute, July 2018
3. Discussant remarks: Krieger, Li, Papanikolaou "Developing Novel Drugs" NBER Entrepreneurship Working Group Meeting, December 2017
4. Cockburn, I. R. Henderson, and S. Stern "AI and Innovation" NBER Conference on Economics of Artificial Intelligence, Toronto, September 2017
5. Discussant remarks: Tabakovic and Wollman " Effects of Regulatory Capture: Evidence from Patent Examiners", NBER Summer Institute, July 2017
6. Ali, A. and Cockburn, I. "Patent Prosecution and the Timing of Licensing" Searle Center/NWU Conference on Innovation Economics, June 2017.
7. Discussant remarks "Abrams, Acigit, Oz "Patent Trolls: Benign Middleman or Stick-up Artist" Searle Center/NWU Roundtable on Patents and Technology Standards", May 2017.
8. Discussant remarks: K. Bryan "R&D Policy and the Direction of Innovation", NBER Summer Institute, July 2014.
9. Agrawal, A., I. Cockburn, L. Zhang "Deals not done: Sources of failure in the market for ideas", NBER Summer Institute, July 2013.
10. _____, Conference on Patent Use, UK Intellectual Property Office, September 2013.
11. _____, KAIST, August 2014.
12. Cockburn, I. "Costs of Patent Assertion Entities." FTC/DOJ Patent Assertion Entity Activities Workshop, Washington, DC, December 2012.
13. Discussant remarks: M. Gittelman "The revolution that never arrived: Clinical and genetic paradigms in bio-medical discovery."12th Annual Roundtable for Engineering Entrepreneurship Research, Georgia Tech, November 2012.
14. Berndt, E. and Cockburn, I. "An Experimental Price Index for Clinical Trials Research" National Science Foundation/National Academies SciSIP Principal Investigators Conference, September 2012.
15. _____, Bureau of Economic Analysis, US Department of Commerce, Washington DC, May 2013.
16. _____, National Institutes of Health, Washington DC, June 2014.
17. Discussant remarks: Kogan et al. "Technological Innovation, Resource Allocation, and Growth", NBER Productivity, Innovation and Entrepreneurship Program Meeting, March 2012.
18. Discussant remarks: Bresnahan, Yin, and Landvoigt, "Information Acquisition and Consumer Choice" NBER Summer Institute, July 2011
19. Discussant remarks: Hegde and Sampat, "The Political Economy of Publicly-Funded Biomedical Research: Evidence from NIH Allocations for Rare Diseases." NBER Summer Institute, July 2011
20. Discussant remarks: Boudreau and Lakhani "The Confederacy of Software Production: Field Experimental Evidence on Heterogeneous Developers, Tastes for Institutions and Effort." NBER Conference on the 50th Anniversary of the Rate and Direction of Inventive Activity, October 2010.
21. Cockburn, I. and Schankerman, M. "Patents, Price Controls and Global Access to New Drugs". 5th Conference on European Policy on Intellectual Property, Maastricht, October 2010.
22. _____, MIT Sloan School, October 2013.
23. _____, UCLA, January 2014.
24. Discussant remarks: Marx et al. "Regional Disadvantage? Non-Compete Agreements and Brain Drain." NBER Summer Institute, July 2010.
25. Cockburn, I. "Local Innovation Market Structure and Growth." Conference on Knowledge in Organizations, EPFL, Monte Verita, May 2010.
26. Agrawal, A., Cockburn, I . and Oettl, A. "Not Invented Here: Innovation in Company Towns." 3rd Conference on Economics of Innovation and Entrepreneurship, Queens University, May 2010.
27. Berndt, E, Cockburn, I, and Thiers, F. "Characterizing the Global Landscape of Clinical Investigation." Office of Health Economics, May 2010.

28. Cockburn, I. and MacGarvie, M. "Patent Thickets and Entry in Software." KU Leuven, December 2009
29. Discussant remarks: Heidi Williams "IPRs and Innovation: Evidence from the Human Genome", NBER Productivity and Technical Change Program Meeting, Cambridge MA December 2009.
30. Cockburn, I. "R&D Productivity in Biopharmaceuticals: Picking Apart the Numbers." R&D Leaders Forum, Boston MA, November 2009.
31. Cockburn, I. "Finding the Endless Frontier: Lessons from the Life Sciences Innovation System for Energy R&D." Conference on Accelerating Energy Innovation: Lessons from Multiple Sectors, National Press Club, Washington DC, October 2009.
32. Cockburn, I. "Patent Thickets." Conference on Patent Statistics for Decision-makers, European Patent Office, Vienna, October 2009.
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Iain M. Cockburn Testimony 2015-Present

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Datasets

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Purdue Call Notes for Ohio

IQVIA Xponent

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Plaintiffs' Medical Claims

Plaintiffs' Pharmacy Claims

Centers for Disease Control and Prevention, Wide-ranging Online Data for Epidemiologic Research (WONDER) Multiple Cause of Death Data

Centers for Disease Control and Prevention, National Ambulatory Medical Care Survey (NAMCS)

Census National Population

National and Ohio Rainfall

Cleveland Sport Team Wins

United States Zip Codes.org Geographic Data

SAS Zipcode Dataset

Depositions

Deposition and Exhibits of G. Caleb Alexander	April 26, 2019
Deposition and Exhibits of David Cutler	April 26–27, 2019
Deposition and Exhibits of Thomas Gilson	January 14, 2019
Deposition and Exhibits of Gary Gingell	November 20, 2018
Deposition and Exhibits of Gary Guenther	October 16, 2018
Deposition and Exhibits of J. David Haddox	February 8, 2019
Deposition and Exhibits of Shannon Hugh	January 15, 2019
Deposition and Exhibits of Greta Johnson	January 15, 2019
Deposition and Exhibits of Margaret Keenan	December 12, 2018

Document Title, Bates Numbers	Document Date
Deposition and Exhibits of David A. Kessler	April 26, 2019
Deposition and Exhibits of Lisa Kohler	July 31, 2018
Deposition and Exhibits of Jeffrey Liebman	May 3, 2019
Deposition and Exhibits of Thomas G. McGuire	April 23 and 30, 2019
Deposition and Exhibits of Meredith B. Rosenthal	May 4–5, 2019
Deposition and Exhibits of Cynthia G. Weiskittel	November 13, 2018
Expert Reports	
Expert Report and Production of G. Caleb Alexander, MD, MS	March 24, 2019
Supplemental Expert Report and Production of G. Caleb Alexander, MD, MS	April 3, 2019
Update to the Supplemental Expert Report and Production of G. Caleb Alexander, MD, MS	April 17, 2019
Expert Report and Production of Professor David Cutler	March 25, 2019
Expert Report and Production of Professor David Egilman	March 25, 2019
Expert Report and Production of Professor Jonathan Gruber	March 25, 2019
Expert Report and Production of Dr. David Kessler	March 26, 2019
Expert Report and Production of Professor Thomas McGuire, Damages to Bellwethers	March 25, 2019
Expert Report and Production of Professor Thomas McGuire, Regarding Public Nuisance	March 25, 2019
Expert Report and Production of Anna Lembke, M.D.	March 25, 2019
Expert Report and Production of Dr. Jeffrey B. Liebman	March 25, 2019
Supplemental Expert Report and Production of Dr. Jeffrey B. Liebman	April 3, 2019
Expert Report and Production of Professor Matthew Perri	March 25, 2019
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Exhibit 1
Ohio County-Level Direct Model of Prescription Opioid Shipments

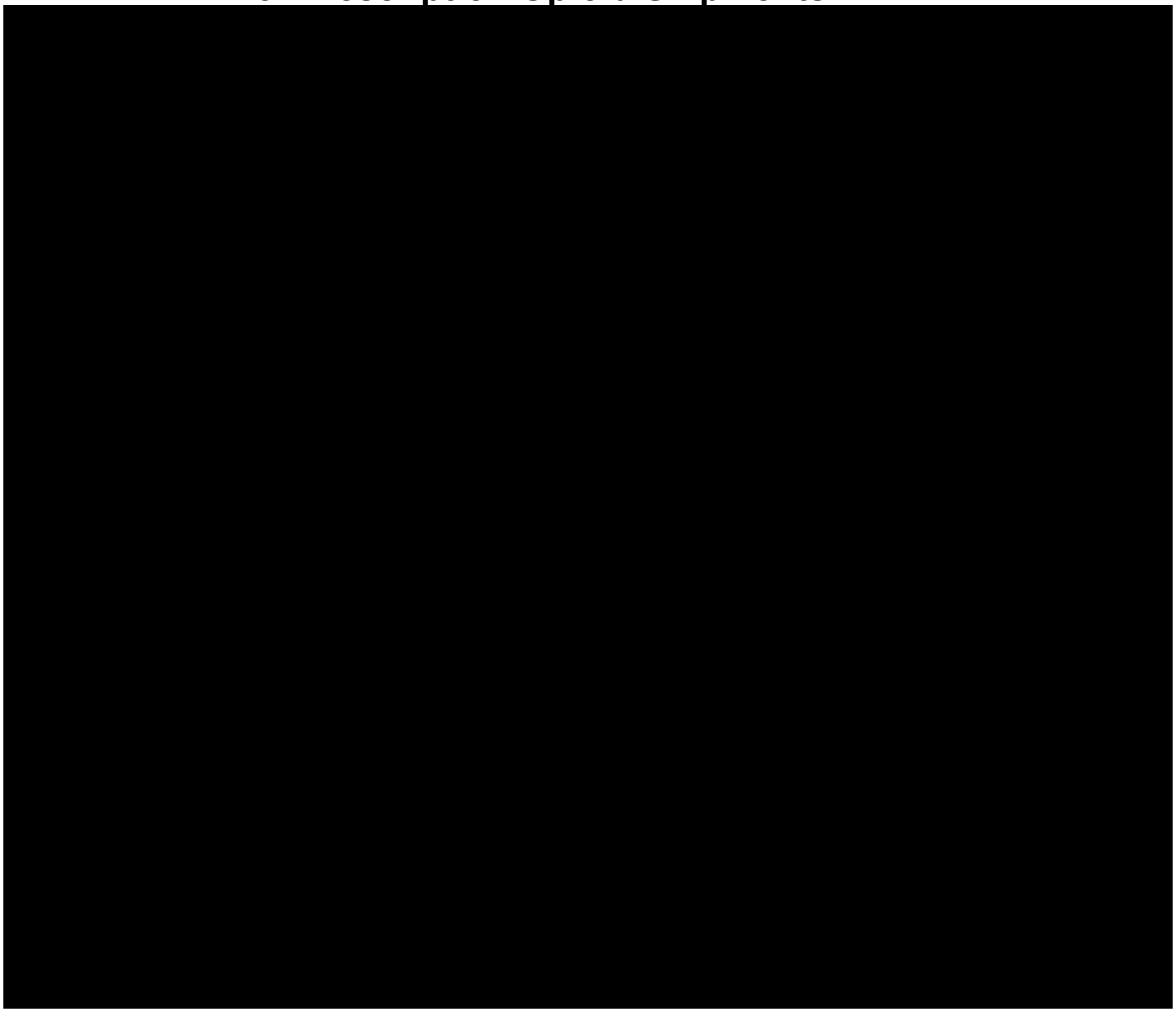

Exhibit 2
Cutler Direct Regression Model
Accounting for Despair Proxy

Coefficients / Regression Information	Outcome: Opioid-Related Mortality Rate	
	Cutler	Cutler + Despair Proxy
	(1)	(2)
Coefficients		
Prescription Opioid Shipments per Capita per Day, 1997–2010	4.39***	2.06***
	(0.60)	(0.56)
Non-Opioid-Related "Deaths of Despair" Rate, 1993–1995 Average		0.55***
		(0.06)
Non-Opioid-Related "Deaths of Despair" Rate, Change from 1993–1995 to 2009–2010		0.36***
		(0.05)
Regression Information		
Cutler Economic and Demographic Controls	X	X
Observations (counties)	400	400
Adjusted R-Squared	0.570	0.688

Source: Cutler Report Production; Case and Deaton (2015, 2017); CDC WONDER Multiple Cause of Death Data

Note: The despair proxy, which is the non-opioid-related "deaths of despair" rate, is calculated in two steps. First, the "deaths of despair" rate is calculated using the NVSS data Professor Cutler produced for years 1993–1995 and CDC Wonder data for years 2009–2010. "Deaths of despair" are defined according to the underlying "deaths of despair" cause of death codes in Case and Deaton (2017). Second, Professor Cutler's opioid-related mortality rate is subtracted from the "deaths of despair" rate to arrive at the non-opioid-related "deaths of despair" rate. *** indicates statistical significance at the 1% level.